

TRADE SECRET

FINAL REPORT

Volume 1 of 4

(Text, Figures 1-4, Tables 1-46 and Appendix A [Tables A1-A5])

STUDY TITLE

A 28-DAY ORAL (Gavage) TOXICITY STUDY
OF H-28397 IN MICE WITH A 28-DAY RECOVERY

STUDY NUMBER

WIL-189207

DATA REQUIREMENT

OECD Guideline 407

STUDY DIRECTOR

Matthew C. Haas, BA, LAT

STUDY INITIATION DATE

3 December 2007

STUDY COMPLETION DATE

29 August 2008

PERFORMING LABORATORY

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SPONSOR WORK REQUEST, SERVICE CODE

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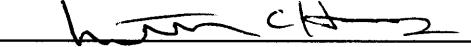
SPONSOR

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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with the United States Environmental Protection Agency (EPA) Good Laboratory Practice Standards (GLP) [40 CFR 792], which are compatible with current OECD Good Laboratory Practices.

Study Director:



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QUALITY ASSURANCE UNIT STATEMENT

Phases Inspected

Date(s) of Inspection(s)	Phase Inspected	Date(s) Findings Reported to Study Director	Date(s) Findings Reported to WIL Management	Auditor(s)
17-Dec-2007	Test Article Preparation	17-Dec-2007	17-Jan-2008	L.Weinstock
18-Dec-2007	Test Article Administration	18-Dec-2007	17-Jan-2008	C.Heifner
10-Jan-2008	Animal Care / Equipment	10-Jan-2008	28-Feb-2008	A.Lowell
15-Jan-2008	Blood Collection and Analysis	15-Jan-2008	28-Feb-2008	M.Salyers
15-Jan-2008	Necropsy	15-Jan-2008	28-Feb-2008	M.Salyers
22-Jan-2008	Body Weights/Food Weights	22-Jan-2008	28-Feb-2008	C.Heifner
08-Apr-2008				
09-Apr-2008				
10-Apr-2008	Study Records (A-1, A-2, A-3)	10-Apr-2008	20-May-2008	M.Stauffer
15-Apr-2008	Study Records (N-1,N-2)	15-Apr-2008	20-May-2008	L.Goodrich
13-May-2008				
14-May-2008	Study Records (I-1,2)	14-May-2008	23-June-2008	D.Little
14-May-2008	Study Records (Rx-1)	14-May-2008	23-June-2008	D.Little
14-May-2008	Study Records (P-1)	14-May-2008	23-June-2008	D.Little
14-May-2008	Study Records (C-1,2,3)	14-May-2008	23-June-2008	D.Little
14-May-2008				
19-May-2008	Draft Report - Excluding App. B, C, H, I	19-May-2008	23-June-2008	D.Little
19-May-2008	Draft Pathology Report	19-May-2008	23-June-2008	D.Little
22-May-2008	Draft Report (Analytical Appendix)			
23-May-2008		23-May-2008	23-June-2008	M.Stauffer

This study was inspected in accordance with the U.S. EPA Good Laboratory Practice Regulations (40 CFR Part 792), the OECD Principles of Good Laboratory Practice, the standard operating procedures of WIL Research Laboratories, LLC, and the sponsor's protocol and protocol amendments with the following exception. The data located in Appendices B (Certificate of Analysis) and I (Liver Metabolic Enzyme Analyses) were the responsibility of the sponsor. Quality Assurance findings, derived from the inspections during the conduct of the study and from the inspections of the raw data and draft report, are

documented and have been reported to the study director. A status report is submitted to management monthly.

This report accurately reflects the data generated during the study. The methods and procedures used in the study were those specified in the protocol, its amendments and the standard operating procedures of WIL Research Laboratories, LLC.

The raw data, the retention sample and the final report will be stored in the Archives at WIL Research Laboratories, LLC, or another location specified by the sponsor.

Approval

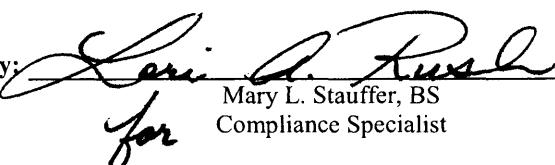
This study was inspected according to the criteria discussed in the Quality Assurance Unit Statement.

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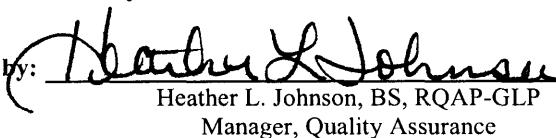
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STUDY INFORMATION

Substance Tested: • FRD-902
• 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid, ammonium salt
• 62037-80-3 (CAS Number)

Haskell Number: 28397

Composition: 88% HFPO Dimer Acid Ammonium Salt
13.3% Water
3.4 ppm Perfluoroctanoic acid

Purity: 88%

Physical Characteristics: Clear and colorless liquid

Study Initiated/Completed: 3 December 2007 / 29 August 2008

Experimental Start/Termination: 18 December 2007 / 10 April 2008

SUMMARY

A. Objective

The objectives of this study were to evaluate the potential toxicity, and recovery there from, of H-28397 when administered to mice by oral gavage for 28 consecutive days.

B. Test Guidelines

The protocol was designed to be in compliance with the United States Environmental Protection Agency (EPA) Good Laboratory Practice Regulations (40 CFR Part 792), 18 September 1989, the Organization for Economic Co-operation and Development Principles of Good Laboratory Practice [C/97 186/Final] and the Organization for Economic Cooperation and Development (OECD) Guidelines for Testing of Chemicals, Health Effects Test Guidelines, Section 407, Repeated Dose 28-Day Oral Toxicity Study in Rodents, adopted 27 July 1995.

C. Study Design

The test substance, H-28397 in the vehicle, deionized water, was administered orally by gavage once daily for a minimum of 28 consecutive days to 3 groups (Groups 2-4) of Crl:CD1(ICR) mice. Dosage levels were 0.1, 3 and 30 mg/kg/day. A concurrent control group (Group 1) received the vehicle on a comparable regimen. The dose volume was 10 mL/kg for all groups with the exception of Group 3, which received a dose volume of 12 mL/kg during study week 0. Groups 1 and 4 each consisted of 20 animals/sex and Groups 2 and 3 each consisted of 10 animals/sex. Following 28 days of dose administration, 10 mice/sex/group were euthanized; the remaining \leq 10 mice/sex in the control and high dose groups were euthanized following a 28-day nondosing (recovery) period.

All animals were observed twice daily for mortality and moribundity. Clinical examinations were performed daily, and detailed physical examinations were performed weekly. Individual body weights and food consumption were recorded weekly. Clinical pathology evaluations (hematology and serum chemistry) were performed on all mice, on the day of their scheduled necropsy, at the primary (study week 4) and recovery (study week 8) necropsies. Complete necropsies were conducted on all animals, and selected organs were weighed at the scheduled necropsies. Selected tissues were examined microscopically from all animals. Sections of the livers from all mice were collected at the scheduled necropsies for total cytochrome P450 and beta-oxidation activity determinations.

D. Results

There were 2 unscheduled deaths during the course of this study. Female no. 91015 (Group 1, 0 mg/kg/day) was found dead on study day 25 and female no. 90987 (Group 4, 30 mg/kg/day)

was found dead on study day 9. Based on clinical observations, gross necropsy observations and histologic findings, the causes of death for these 2 animals were undetermined. However, the lack of a dose- and/or time-related response suggests that these deaths were not related to the test substance.

There were no significant clinical observations noted throughout the study. Cumulative body weights were significantly higher compared to controls in the 30 mg/kg/day group males and females at the end of the dosing period, which correlates with the significantly higher liver weights noted for these animals. Body weight gain slowed for these animals during the recovery period and body weights in the 30 mg/kg/day animals were comparable to the control group by the end of the study. Food consumption was slightly higher in the 30 mg/kg/day males and females during the dosing period but was generally comparable to the control group throughout the recovery period.

There were no alterations in hematologic parameters that were considered adverse. Statistically significant, test substance-related decreases in red cell mass parameters (red blood cells, hemoglobin and/or hematocrit) were present in the 3 and 30 mg/kg/day group males. The changes in red cell mass parameters were minimal (decreased less than 10% compared to controls). Based on the minimal nature of these changes in erythron, and on the observation that the changes showed recovery by study week 8, they were not considered to be adverse. In females, no effect on red cell mass was evident.

Test substance-related serum chemistry findings included changes in liver enzymes and serum proteins in males and females administered 3 or 30 mg/kg/day. Liver enzyme levels (alanine aminotransferase, alkaline phosphatase and sorbitol dehydrogenase) were higher in the 3 and 30 mg/kg/day group males and 30 mg/kg/day group females at study week 4. Aspartate aminotransferase levels were also higher in the 3 and 30 mg/kg/day group males at study week 4. These liver enzyme level changes were consistent with hepatocellular injury, and single cell necrosis was noted microscopically in some animals in these groups. Liver enzyme changes were reversible in both males and females, as levels for all liver enzymes were similar to controls following 4 weeks of recovery. Minimal changes of higher albumin, lower globulin, and associated changes of increased total protein and increased albumin/globulin ratio were present in the 30 mg/kg/day group males. Decreased globulin and increased albumin/globulin ratio were also present in the 3 mg/kg/day group males. A similar pattern of change in serum proteins was present in females administered 3 or 30 mg/kg/day. These serum protein changes were reversible, as there were no statistically significant changes in these parameters in males or females by study week 8. Blood urea nitrogen was slightly increased in the 30 mg/kg/day group males at the end of exposure. Blood urea nitrogen was similar to control values following the 4-week recovery period. The slight increase in urea nitrogen in 30 mg/kg/day group males was not associated with changes in related clinical chemistry parameters or with test substance-related microscopic findings in the kidney and was thus considered to be nonadverse.

A statistically significant decrease in cholesterol was present in the 3 mg/kg/day group males. This decrease was not dose-related, as mean cholesterol in the 30 mg/kg/day group males was not statistically different from controls and was higher than that of the 3 mg/kg/day group males. However, several individual cholesterol values in treated male groups were below the study control range, and thus, a test substance-related effect of decreased cholesterol can not be ruled

out. However, individual cholesterol values in treated groups were within the WIL historical control values (with the exception of 1 male in the 3 mg/kg/day group), and thus changes in cholesterol were not considered to be adverse.

Test substance-related gross necropsy findings included enlarged liver in the 30 mg/kg/day group males at the primary necropsy. There were no test substance-related gross necropsy findings at the recovery necropsy.

Liver weights were increased in the 3 and 30 mg/kg/day group males and females at the end of the exposure period. These changes correlated with hepatocellular hypertrophy microscopically and with increases in beta-oxidation. Liver weights were mostly, but not completely, reversible in the 30 mg/kg/day males and females. At this dose, liver weight relative to body weight in the 30 mg/kg/day group males was increased by 163.1% above controls at the end of exposure, and was reduced to 21.5% of control after the 4-week recovery period. Similarly, in 30 mg/kg/day group females, liver weight relative to body weight was increased by 102.7% above controls at the end of exposure and was reduced to 14.3% of control after the 4-week recovery period.

Adrenal gland weights (absolute and relative to body and brain weights) were increased in the 3 and 30 mg/kg/day group males at the end of the exposure period. In the 30 mg/kg/day group males, these adrenal weight changes correlated with minimal adrenal cortical hypertrophy microscopically. Adrenal weight changes were reversible following the 4-week recovery period. Decreased uterus weights (absolute and relative to body and brain weights) were present in the 30 mg/kg/day group females at the end of the exposure period. There were no histopathological changes in the uterus that were correlative to the uterine weight changes. There were no other test substance-related effects on organ weights.

Minimal adrenal cortical hypertrophy was observed microscopically in the 30 mg/kg/day group males at the primary necropsy. This change correlated with increased adrenal weights in this group. Adrenal cortical hypertrophy was not observed in the 30 mg/kg/day group males at the recovery necropsy.

Hepatocellular hypertrophy was observed in the 3 and 30 mg/kg/day group males and females at the primary necropsy. This change was consistent with increased liver weights noted in these groups. The hepatocellular hypertrophy was characterized by expansion of the hepatocellular cytoplasm by numerous fine eosinophilic granules. Other findings in the liver included multifocal single cell hepatocellular necrosis in the 3 and 30 mg/kg/day group males and 30 mg/kg/day group females at the primary necropsy, and increased mitoses distributed multifocally throughout the liver section in the 30 mg/kg/day group males and females at the primary necropsy. Incidences of these changes were higher in the males compared to the females. Hepatocellular hypertrophy, single cell hepatocellular necrosis and increased mitoses in the liver were not observed in the 30 mg/kg/day group males and females at the recovery necropsy.

There was an increased number of animals in the diestrus stage of the estrous cycle in the 30 mg/kg/day group females compared to control group females at the primary necropsy. However, ovarian morphology, including number and maturational stages of corpora lutea were similar between treated and control groups, suggesting normal estrous cycling. Therefore, the significance of the differences in estrous stage distribution between the 30 mg/kg/day group

females and control group females is uncertain. The number of animals in the diestrus stage of the estrous cycle was equal in the control and 30 mg/kg/day group females at the recovery necropsy.

The test substance was an inducer of hepatic peroxisomal beta-oxidation activity, a measure of peroxisome proliferation, in male mice after administration of 0.1, 3 and 30 mg/kg/day and in female mice after administration of 3 and 30 mg/kg/day for 28 days. Total hepatic microsomal cytochrome P-450 enzyme content was decreased at a dosage of 3 and 30 mg/kg/day in male mice but not in females. Beta-oxidation activity in both male and female mice had returned to control levels after approximately 28 days of recovery, while total cytochrome P-450 content remained below control levels in the males.

E. Conclusions

Based on the results of this study, H-28397 administered orally (gavage) to Crl:CD1(ICR) mice at dosage levels of 0.1, 3 and 30 mg/kg/day for 28 consecutive days was well tolerated. Most test substance-related effects were consistent with a peroxisome proliferator (PPAR α agonist) and included increased beta-oxidation in the liver, increased liver weights, hepatocellular hypertrophy, and changes in serum lipids and proteins. Other changes included increased body weights, minimal decreases in red cell mass parameters and increased adrenal weights and adrenal cortical hypertrophy. These effects were reversible following a 4-week recovery period. Adverse effects were noted in the livers of males at 3 mg/kg/day and above and females at 30 mg/kg/day. These consisted of single cell necrosis of hepatocytes and correlative increases in liver enzymes. These effects were also reversible following the 4-week recovery period. Therefore, the no-observed-adverse-effect level (NOAEL) for oral (gavage) administration of H-28397 to Crl:CD1(ICR) mice for 28 consecutive days was 0.1 mg/kg/day for males and 3 mg/kg/day for females.

INTRODUCTION

A. General Study Information

This report presents the data from “A 28-Day Oral (Gavage) Toxicity Study of H-28397 in Mice with a 28-Day Recovery”. Due to software spacing constraints, the study title appears as “A 28-Day Oral Study of H-28397 in Mice” on the report tables. On 15 February 2008, Matthew C. Haas, BA, LAT assumed the role of study director originally held by Michael S. Koch, PhD.

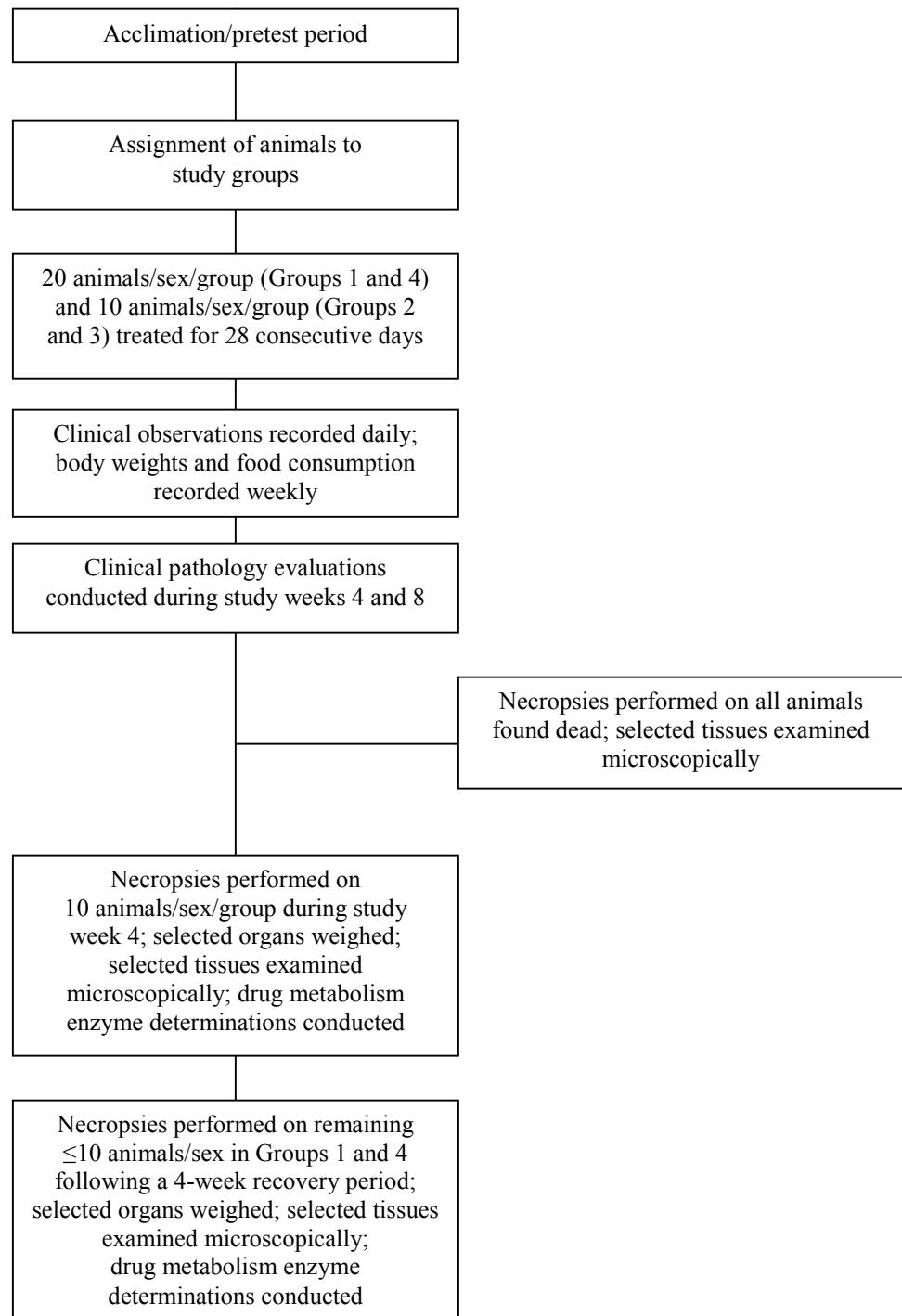
The following computer protocol was used for data collection during the study:

<u>Computer Protocol(s)</u>	<u>Type of Data Collected</u>
WIL-189207M.....	Main study data (Males)
WIL-189207F	Main study data (Females)
WIL-189207H	Recovery period data (Males)
WIL-189207W	Recovery period data (Females)
WIL-189207V	Unscheduled data (Females)
WIL-189207P	Pretest data

B. Key Study Dates

<u>Date(s)</u>	<u>Event(s)</u>
4 December 2007.....	Experimental starting date (animal receipt)
14 December 2007.....	Assignment to study groups
18 December 2007.....	Experimental start date (initiation of dose administration for males; study day 0)
19 December 2007.....	Initiation of dose administration for females (study day 0)
15 January 2008.....	Primary necropsy (males; study week 4)
16 January 2008.....	Primary necropsy (females; study week 4)
14 February 2008.....	Recovery necropsy (study week 8)
10 April 2008.....	Experimental termination (completion) date (last histopathological examination)

STUDY DESIGN



EXPERIMENTAL PROCEDURES - MATERIALS AND METHODS

A. Test Substance And Vehicle

1. Test Substance Identification

The test substance, H-28397, was received from E.I. du Pont de Nemours and Company, Newark, Delaware, on 2 November 2007, as follows:

<u>Identification</u>	<u>Quantity Received</u>	<u>Physical Description</u>
H-28397	2 bottles	Clear, colorless
Lot/Batch no. E1131181-19-B	Total gross weight:	liquid
Retest date: 16 November 2008	2787.0 g	
[WIL log no. 7741A]		

Documentation regarding the purity and stability of the test substance is on file with the sponsor and WIL Research Laboratories, LLC. A Certificate of Analysis for the test substance was provided by the sponsor and is presented in Appendix B. The purity of the test substance was 88%. The test substance was stored at room temperature, and was considered stable under this condition. A reserve sample of the test substance (approximately 1 g) was collected on 9 November 2007, and stored in the Archives of WIL Research Laboratories, LLC.

2. Vehicle Identification

The vehicle used in preparation of the test substance formulations and for administration to the control group was deionized water (prepared on-site).

3. Preparation

Dosing formulations were prepared at the concentrations indicated in the following table:

<u>Group Number</u>	<u>Test Substance</u>	<u>Dosage Level (mg/kg/day)</u>	<u>Test Substance Concentration (mg/mL)^a</u>
2	H-28397	0.1	0.01
3	H-28397	3	0.3
4	H-28397	30	3

^a = Test substance formulations were adjusted by a factor of 1.14 to account for test substance purity.

The stock solution (30 mg/mL) was prepared as follows. The appropriate amount of the test substance was weighed into a calibrated glass container. Vehicle was added to bring the formulation to approximately 70% of the required volume. The formulation was mixed until uniform using a magnetic stirrer. Vehicle was then added to bring the formulation to the calibration mark and the formulation was refrigerated and stirred overnight.

The dosing formulations were prepared as follows. Deionized water was placed into a calibrated glass container for each formulation. An appropriate amount of stock solution was added to each container to bring the formulations to approximately 70% of the calibration mark. The formulations were mixed until uniform using a magnetic stirrer. Vehicle was then added to bring the formulation to the calibration mark and the formulation was refrigerated and stirred overnight.

The test substance formulations were prepared approximately weekly as single formulations for each dosage level, divided into aliquots for daily dispensation and stored refrigerated and protected from light. The test substance formulations were stirred continuously throughout the preparation, sampling and dose administration procedures. The pH was measured for the formulations prepared on 17 December 2007; the pH measurements for the 0, 0.01, 0.3 and 3 mg/mL formulations were 6.01, 7.67, 8.27 and 8.42, respectively.

4. Sampling And Analyses

Prior to the initiation of dose administration (13 and 14 December 2007), 0.01 and 3 mg/mL test substance formulations were prepared in volumes required to dose a group of animals for approximately 1 week. Duplicate samples (1 mL each) for homogeneity determination were collected from the top, middle and bottom strata of these formulations on 14 December 2007.

Two sets of quadruplicate samples (1.0 mL each) for resuspension homogeneity and stability determinations were collected, 1 set on 14 December 2007 and 1 set on 26 December 2007, from the top and bottom strata of an aliquot for the 0.01 and 3 mg/mL formulations. One set of aliquots was stored at room temperature for 5 hours and another 2 aliquots were stored refrigerated for 12 days prior to resuspension homogeneity and stability determinations. Backup samples were stored frozen.

Duplicate samples (1 mL each) for concentration analyses were collected from formulations used during study weeks 0, 1 and 3 (including the vehicle formulation administered to the control group).

Two additional 2 mL samples from the bulk pre-initiation formulations (13-14 December 2007) were collected and shipped to the sponsor.

All analyses were conducted by the Analytical Chemistry Department, WIL Research Laboratories, LLC. The methodology and results of these analyses are presented in Appendix C and the results are summarized in Section A of the Results And Discussion section of this report.

B. Test System

Crl:CD-1 mice from Charles River Laboratories, Inc., Raleigh, North Carolina were used as the test system on this study. This species and strain of animal is recognized as appropriate for toxicity studies. The CD-1 mouse was selected because it is a widely used strain for which significant historical control data are available. The animals were approximately 7 weeks old at the initiation of dose administration.

C. Organization Of Test Groups, Dosage Levels And Treatment Regimen

The vehicle and test substance formulations were administered orally by gavage via stainless steel ball-tipped metal and PTFE plastic dosing cannula (Natume, Japan) and plastic syringes of appropriate size once daily for 28 consecutive days, through the day prior to the scheduled primary necropsy. The dose volume for all groups was 10 mL/kg, with the exception of Group 3 which received a dose volume of 12 mL/kg during study week 0. Individual doses were based on the most recently recorded body weights to provide the correct mg/kg/day dosage. Adjusted doses became effective the day after collection of the weekly body weights.

The following table presents the study group assignment:

Group Number	Test Substance	Dosage Level	Dose Volume	Number of Animals ^b	
		(mg/kg/day) ^a	(mL/kg)	Males	Females
1	Vehicle	0	10	20	20
2	H-28397	0.1	10	10	10
3	H-28397	3	10 ^c	10	10
4	H-28397	30	10	20	20

^a = Test substance formulations were adjusted by a factor of 1.14 to account for test substance purity.

^b = 10 animals/sex/group were euthanized following a minimum of 28 days of dose administration; the remaining 10 animals/sex/group were euthanized following a 28-day nondosing (recovery) period.

^c = Due to lower than acceptable suspension formulation concentrations, the dose volume was increased to 12 mL/kg for Group 3 during study week 0 to ensure that animals received protocol-specified dosage levels. For the remainder of the dosing period, the dosage volume was 10 mL/kg as the dosing formulations prepared from study week 1 to the end of the study were within the specified target range.

Dosage levels were selected by the sponsor based on existing data for this test substance.

The selected route of administration for this study was oral (gavage) because further potential testing will be conducted by the oral route. The number of animals selected for this study was the minimum required to yield statistically and scientifically meaningful data and was consistent with regulatory agency expectations.

D. Animal Receipt And Acclimation/Pretest Period

Seventy male and 70 female Crl:CD-1 mice were received in good health on 4 December 2007, from Charles River Laboratories, Inc., Raleigh, North Carolina. The animals were approximately 37 days old at receipt. Each animal was examined by a qualified technician on the day of receipt and weighed 3 days later. Each animal was uniquely identified by a Monel® metal ear tag displaying the permanent identification number. All animals were housed for a 14-day acclimation/pretest period. During this period, each animal was observed twice daily for mortality and changes in general appearance or behavior.

Pretest data collection began on 7 December 2007. Individual body weights were recorded and detailed physical examinations were performed periodically during the pretest period. Food consumption data were also recorded for pretest animals prior to the initiation of dose administration. Pretest clinical observations are presented in Appendix D.

E. Animal Housing

Upon arrival, all animals were housed 2 or 3 per cage by sex for approximately 3 days. Thereafter, all animals were housed individually in clean, stainless steel, wire-mesh cages suspended above cage-board. Animals were maintained in accordance with the *Guide for the Care and Use of Laboratory Animals* (National Research Council, 1996). The animal facilities at WIL Research Laboratories, LLC are accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International).

F. Diet, Drinking Water And Maintenance

The basal diet used in this study, PMI Nutrition International, LLC, Certified Rodent LabDiet® 5002 (meal), is a certified feed with appropriate analyses performed by the manufacturer and provided to WIL Research Laboratories, LLC. Reverse osmosis-treated (on-site) drinking water, delivered by an automatic watering system, and the basal diet were provided ad libitum throughout the study. Municipal water supplying the facility was analyzed for contaminants according to the standard operating procedures. The results of the diet and water analyses are maintained at WIL Research Laboratories, LLC and in the study records. No contaminants were present in animal feed or water at concentrations sufficient to interfere with the objectives of this study.

G. Environmental Conditions

All animals were housed throughout the acclimation period and during the study in an environmentally controlled room. The room temperature and humidity controls were set to maintain daily averages of $71 \pm 5^{\circ}\text{F}$ ($22 \pm 3^{\circ}\text{C}$) and $50 \pm 20\%$ relative humidity. Room temperature and relative humidity were controlled and monitored using the Metasys® DDC Electronic Environmental control system. These data were recorded approximately hourly and are summarized in Appendix F. Actual mean daily temperature ranged from 70.1°F to 70.7°F (21.2°C to 21.5°C) and mean daily relative humidity ranged from 35.5% to 50.0% during the study. Fluorescent lighting provided illumination for a 12-hour light (0600 hours to 1800 hours)/12-hour dark photoperiod. The 12-hour light/12-hour dark photoperiod was interrupted as necessary to allow for the performance of protocol-specified activities. Air handling units were set to provide a minimum of 10 fresh air changes per hour.

H. Assignment Of Animals To Treatment Groups

On 14 December 2007 (4 days prior to the initiation of dose administration), all available mice were weighed and examined in detail for physical abnormalities. These data were collected using the WIL Toxicology Data Management System (WTDMSTM) and reviewed by the study director. The animals judged suitable for assignment to the study were selected for use in a computerized randomization procedure. A printout containing the animal numbers, corresponding body weights and individual group assignments was generated based on body weight stratification in a block design. The animals were then arranged into groups according to

the printout. Individual body weights at randomization were within \pm 20% of the mean for each sex. The control and 30 mg/kg/day groups (Groups 1 and 4, respectively) each consisted of 20 males and 20 females, and the 0.1 and 3 mg/kg/day groups (Groups 2 and 3, respectively) each consisted of 10 males and 10 females. Individual body weights ranged from 25.8 g to 36.3 g for males and from 20.9 g to 27.5 g for females at the initiation of dosing.

PARAMETERS EVALUATED

A. Clinical Observations And Mortality

Clinical examinations were performed twice daily, at the time of dosing and approximately 1 to 2 hours following dose administration. During the recovery period, the animals were observed once daily. The absence or presence of findings was recorded for individual animals at the scheduled intervals. Detailed physical examinations were conducted on all animals weekly, beginning 2 weeks prior to test substance administration and prior to the scheduled necropsies. During the recovery period, daily clinical observations may not have been performed on days when detailed physical examinations were conducted. Any observations noted outside of the above-specified intervals were also recorded and are presented in Appendix E.

B. Body Weights

Individual body weights were recorded at least weekly, beginning 2 weeks prior to test substance administration (study week -2). Mean body weights and mean body weight changes were calculated for the corresponding intervals. Final body weights were recorded prior to the scheduled necropsies for animals.

C. Food Consumption

Individual food consumption was recorded weekly, beginning 2 weeks prior to test substance administration (study week -2 to -1). Food intake was calculated as g/animal/day for the corresponding body weight intervals.

D. Clinical Pathology

Blood samples for clinical pathology evaluations (hematology and serum chemistry) were collected from all animals at the scheduled necropsies (study weeks 4 and 8). Blood was collected for hematology and serum chemistry evaluation via the retro-orbital sinus of animals anesthetized by inhalation of isoflurane. Blood was collected into tubes containing potassium EDTA (hematology) or no anticoagulant (serum chemistry). The target volumes of blood samples for serum chemistry and hematology analyses were 0.6 and 0.3 mL, respectively. In the event that an insufficient volume of blood was collected, priority was given to the analysis of serum chemistry parameters. Clinical pathology methods, procedures and references are presented in Appendix G. Interpretation of the clinical pathology data was performed by Ellen L. Ziemer, DVM, PhD, DACVIM, DACVP (Appendix H). The following parameters were evaluated:

1. Hematology

Total leukocyte count (White Cells)	Differential leukocyte count -
Erythrocyte count (Red Cells)	Percent and absolute
Hemoglobin	-Neutrophil
Hematocrit	-Lymphocyte
Mean corpuscular volume (MCV)	-Monocyte
Mean corpuscular hemoglobin (MCH)	-Eosinophil
Mean corpuscular hemoglobin concentration (MCHC)	-Basophil
Platelet count (Platelet)	-Large unstained cell
Reticulocyte count	Blood smears ^a
Percent (Reticulocyte)	
Absolute (Retic Absolute)	

() - Designates tabular abbreviation

^a - Blood smears were evaluated if scientifically warranted. Parameters evaluated from these smears included a differential leukocyte count, platelet estimates and RBC morphology.

2. Serum Chemistry

Total cholesterol (Cholesterol)	Aspartate aminotransferase
Triglycerides (Triglyceride)	(AspartatTransfer)
Sorbitol dehydrogenase (Sorbitol'Genase) ^a	Urea nitrogen
Alanine aminotransferase (Alanine Transfer)	Creatinine
Alkaline phosphatase (AlkalinePhos'tse)	Glucose
Total bilirubin (Total Bili)	Calcium
Total protein	Sodium
Albumin	Potassium
Globulin [by calculation]	Chloride
Albumin/globulin ratio (A/G Ratio) [by calculation]	Phosphorus

() - Designates tabular abbreviation

^a - Presented on special chemistry tables

Note: serum chemistry parameters are listed in order of priority for analysis

E. Anatomic Pathology

1. Macroscopic Examination

A complete necropsy was conducted on all animals found dead and at the scheduled necropsies. Animals were euthanized by carbon dioxide anesthesia and exsanguinated. The necropsies included, but were not limited to, examination of the external surface, all orifices, and the cranial, thoracic, abdominal and pelvic cavities, including viscera. Clinical findings that were confirmed macroscopically were designated CEO (correlates with externally observed) on the individual macroscopic data tables. The following tissues and organs were collected and placed in 10% neutral-buffered formalin (except as noted):

Adrenals (2)	Lungs (including bronchi, fixed by inflation with fixative)
Aorta	Lymph nodes
Bone with marrow	Mandibular
Femur	Mesenteric
Sternum	Nasal cavity ^e
Bone marrow smear ^a	Ovaries (2) with oviducts ^f
Brain	Pancreas
Cerebrum (2 levels)	Peripheral nerve (sciatic)
Cerebellum with pons/medulla	Pharynx
Cervix	Pituitary
Epididymides (2) ^b	Prostate
Exorbital lacrimal glands (2)	Salivary glands [mandibular (2)]
Eyes with optic nerve (2) ^c	Seminal vesicles (2)
Gallbladder	Skeletal muscle (rectus femoris)
Gastrointestinal tract	Skin with mammary gland ^g
Esophagus	Spinal cord (cervical, thoracic, lumbar)
Stomach	Spleen
Duodenum	Testes (2) ^b
Jejunum	Thymus
Ileum	Thyroids [with parathyroids (2)] ^f
Peyer's patches	Tongue
Cecum	Trachea
Colon	Urinary bladder
Rectum	Uterus and vagina
Heart	Gross lesions and masses(when possible)
Kidneys (2)	
Larynx	
Liver ^d	

^a - Bone marrow smears were obtained at the scheduled necropsies but not placed in formalin.

^b - Fixed in Bouin's solution

^c - Fixed in Davidson's solution

^d - Representative cross-sections were collected from the left and median lobes at the time of necropsy and fixed in 10% neutral-buffered formalin. The remaining liver tissue was collected for liver metabolic enzyme analysis as indicated in Section F.

^e - Levels I and III were examined using the method of Young (1981).

^f - Oviducts and parathyroids were examined microscopically when in the plane of section and in all cases where a gross lesion was present.

^g - For females; a corresponding section of skin was collected from the same anatomic area for males.

2. Organ Weights

The following organs were weighed from all animals at the scheduled necropsies:

Adrenals	Ovaries (with oviducts)
Brain	Spleen
Epididymides	Testes
Heart	Thymus
Kidneys	Uterus
Liver	

Paired organs were weighed together. Organ-to-final-body-weight and organ-to-brain-weight ratios were calculated.

3. Microscopic Examination

After fixation, protocol-specified tissues were shipped to Biotechnics, Inc. (a division of WIL Research Laboratories, LLC), Hillsborough, North Carolina, for processing. The tissues were trimmed according to Biotechnics' standard operating procedures and the protocol. Trimmed tissues were processed into paraffin blocks, sectioned at 4 to 6 microns, mounted on glass microscope slides and stained with hematoxylin and eosin.

Microscopic examination was performed on all tissues listed in Section E.1. from all animals found dead and at the scheduled necropsies from animals in Groups 1 and 4. In addition, potential target tissues (the liver, adrenal glands, ovaries with oviducts, cervix, uterus and vagina) were examined from Group 2 and 3 animals euthanized at the primary necropsy and Group 1 and 4 animals at the recovery necropsy. Tissues may appear on the report tables as not examined due to the tissue not being in the plane of section, not present at trimming, etc. Microscopic examination was performed by Amera Remick, DVM, DACVP, WIL Research Laboratories, LLC (Appendix H).

F. Liver Metabolic Enzyme Analysis

Following collection of the organ weights for all animals euthanized at the scheduled necropsies, an approximate 1-gram section of liver (the entire right and caudate lobes and the tissue remaining from the left and median lobes after cross-sections were taken for histopathological examination) was collected. The liver tissue was then rinsed in chilled saline, placed in a cryovial, flash frozen in liquid nitrogen and stored frozen (approximately -60° to -80°C) until shipment on dry ice via overnight courier to DuPont Haskell Global Centers for Health and Environmental Sciences, Newark, Delaware, for analysis. Results of the analyses are presented in Appendix I.

G. Statistical Methods

All statistical tests were performed using appropriate computing devices or programs. Analyses were conducted using two-tailed tests (except as noted otherwise) for minimum significance

levels of 1% and 5%, comparing each test substance-treated group to the control group by sex. Significance for liver metabolic analysis was judged at $p < 0.05$. Each mean was presented with the standard deviation (S.D.), standard error (S.E.) and the number of animals (N) used to calculate the mean. In addition, percent difference from the control group is presented for body weights, clinical pathology parameters and organ weights. Statistical analyses were not conducted if the number of animals was 2 or less. Due to the use of significant figures and the different rounding conventions inherent in the types of software used, the means and standard deviations on the summary and individual tables may differ slightly.

Body weight, body weight change, food consumption, clinical pathology and organ weight data were subjected to a parametric one-way analysis of variance (ANOVA) (Snedecor and Cochran, 1980) to determine intergroup differences. If the ANOVA revealed statistically significant ($p < 0.05$) intergroup variance, Dunnett's test (Dunnett, 1964) was used to compare the test substance -treated groups to the control group.

Cytochrome P450 and beta oxidation data were subjected to a preliminary test of homogeneity (Levene, 1960) and normality (Shapiro and Wilk, 1965). If the preliminary test is not significant, one-way analysis of variance (Snedecor and Cochran, 1980) followed by Dunnett's test (Dunnett, 1964; Tamhane, 1979) were performed. If the preliminary test was significant, a Kruskal-Wallis test (Kruskal and Wallis, 1952) followed by Dunn's test (Dunn, 1964) were performed.

H. Data Retention

The Sponsor has title to all documentation records, raw data, specimens, slides or other work product generated during the performance of the study. All work product generated by WIL Research Laboratories, LLC, including raw paper data, pertinent electronic storage media and leftover test substance will be returned to the Sponsor as specified in the study protocol. All specimens will be shipped directly to EPL Archives, Inc., Sterling, Virginia. Data generated by the Sponsor will be archived by the Sponsor or the Sponsor's designee.

A reserve sample of the test substance, pertinent electronic storage media and the original final report are retained in the Archives at WIL Research Laboratories, LLC in compliance with regulatory requirements. All remaining formulation and clinical pathology samples will be discarded upon issuance of the final report.

RESULTS AND DISCUSSION

A. Analytical Chemistry

Analytical Chemistry Report: Appendix C

The results of the homogeneity and the 5-hour and 12-day resuspension homogeneity analyses are summarized in Text Tables 1 through 3.

Text Table 1. Homogeneity Assessment Of The 13-14 December 2007 Formulations

	Group 2 (0.01 mg/mL)	Group 4 (3 mg/mL)
Mean Concentration (mg/mL)	0.0110	3.01
Standard Deviation	0.00095	0.25
Relative Standard Deviation (%)	8.6	8.3
Mean % of Target	110	100

The formulations analyzed met the WIL standard operating procedure (SOP) acceptance criteria for test article homogeneity, i.e., the relative standard deviation (RSD) for the mean concentration was 10% or less at a concentration within the acceptable limits (85% to 115% of target concentration).

Text Table 2. 5-Hour Resuspension Homogeneity Assessment 13-14 December 2007 Formulations

	Group 2 (0.01 mg/mL)	Group 4 (3 mg/mL)
Mean Concentration (mg/mL)	0.0102	2.92
Standard Deviation	0.00038	0.31
Relative Standard Deviation (%)	3.7	11
Mean % of Target	102	97.5

Text Table 3. 12-Day Resuspension Homogeneity Assessment 13-14 December 2007 Formulations

	Group 2 (0.01 mg/mL)	Group 4 (3 mg/mL)
Mean Concentration (mg/mL)	0.0101	2.91
Standard Deviation	0.00069	0.026
Relative Standard Deviation (%)	6.9	0.91
Mean % of Target	101	96.9

The formulations stored at room temperature for 5 hours and 12 days met the WIL SOP acceptance criteria for resuspension homogeneity, i.e., the RSD for the mean concentration was 10% or less, with the following exception. Following 5 hours of room temperature storage, the RSD for the mean concentration of the formulation prepared at 3 mg/mL was 11%. The out-of-specification result was believed to be due to drift in the ionization efficiency of the mass spectrometer. Consequently, the study director evaluated the data and considered it acceptable.

To reduce the variability, the assay was cross-validated with a modified diluent and mobile phases in another study (Haas, 2008) prior to the 12-day resuspension homogeneity assessment.

The stability results are summarized in the following table.

Text Table 4. Stability Assessment Of The 13-14 December 2007 Formulations

Time Point (Storage Condition)	Mean Concentration, mg/mL (% of Pre-Storage)	
	Group 2 (0.01 mg/mL)	Group 4 (3 mg/mL)
5 Hours (Room Temperature)	0.0102 (92.7)	2.92 (97.2)
12 Days (Refrigerated)	0.0101 (91.1)	2.91 (96.6)

The mean post-storage concentrations ranged from 91.1% to 97.2% of the pre-storage values, which met the WIL SOP requirement for stability.

The mean concentrations and percent of target values are summarized in the following table.

Text Table 5. Concentration Assessment

Date of Preparation	Group 1 (0 mg/mL)	Group 2 (0.01 mg/mL)	Group 3 (0.3 mg/mL)	Group 4 (3 mg/mL)
13-14 December 2007*	NA	0.0112 (112)	NA	2.92 (97.4)
17-18 December 2008	ND	0.00864 (86.4)	0.233 (77.8)	3.26 (109)
23 December 2008	ND	0.0108 (108)	0.341 (114)	2.97 (99.1)
7-8 January 2008	ND	0.0110 (110)	0.306 (102)	2.99 (99.7)

ND = No test article chromatographic peak detected

NA = Not Applicable

* = Prepared prior to dosing and not used for dosing

The analyzed formulations used for dose administration met the WIL SOP requirement for concentration acceptability for suspension formulations, i.e., the analyzed concentrations were 85% to 115% of the target concentrations with one exception. The Group 3 formulation prepared on 17-18 December 2007 at the nominal test article concentration of 0.3 mg/mL was 77.8% of target. Consequently, the study director changed the dose volume from 10 mL/kg to 12 mL/kg for that Group 3 formulation. No test article was detected in the vehicle formulation for administration to the control group (Group 1).

B. Clinical Observations And Mortality

Summary Data: Tables 1 through 10

Individual Data: Tables A1 through A10

Two females were found dead during the course of this study. One control group female (no. 91015) was found dead on study day 25, and female no. 90987 (Group 4, 30 mg/kg/day) was found dead on study day 9. There were no significant clinical observations for these animals, and gross necropsy observations were non-conclusive. Therefore, the cause of death for these 2 animals was undetermined. However, the lack of a dose response and/or time-related

response suggests that these deaths were not related to the test substance. All other animals survived to the scheduled necropsies.

All clinical findings in the test substance-treated groups were noted with similar incidence in the control group, were limited to single animals, were not noted in a dose-related manner and/or were common findings for laboratory rats of this age and strain.

C. Body Weights

Summary Data: Tables 11 through 22; Figures 1, 2, 3, 4

Individual Data: Tables A11, A12, A13, A14, A15, A16

Cumulative body weight gains were significantly higher compared to controls in the 30 mg/kg/day group males and females at the end of the dosing period, which likely correlates to the increased liver weight noted at this dosage level. Cumulative body weight gains were also higher, although not significantly so, in the 3 mg/kg/day males and females at the end of the dosing period. During the recovery period, the 30 mg/kg/day males and females were noted with lower body weight gains or losses when compared to the control group animals, which resulted in comparable body weights for both groups by the end of the recovery period; this indicates recovery from test substance administration. There were no effects on body weight in the 0.1 mg/kg/day group males and females.

D. Food Consumption

Summary Data: Tables 23, 24, 25, 26

Individual Data: Tables A17, A18

Food consumption was slightly higher throughout the dosing period for the 30 mg/kg/day males and females. During the recovery period, food consumption was comparable to the control group, with the exception of a single interval during which 30 mg/kg/day group male food consumption was significantly lower than the control group. There were no effects on food consumption in the 0.1 or 3 mg/kg/day group males and females.

E. Clinical Pathology

1. Hematology And Coagulation

Summary Data: Tables 27, 28

Individual Data: Tables A19, A20, A21, A22

Pathology Report: Appendix H

There were no alterations in hematologic parameters that were considered adverse.

Statistically significant decreases in red cell mass parameters (red blood cells, hemoglobin and/or hematocrit) were present in the 3 and 30 mg/kg/day male groups. The changes in red cell mass

parameters were minimal (mean values for all red cell mass parameters in these groups were decreased by approximately 8% or less compared to the respective control values). Based on the minimal nature of these changes, they were not considered to be adverse. Changes in the erythron showed recovery by study week 8. In females, no effect on red cell mass was evident.

A slight increase in monocyte counts was present in the 30 mg/kg/day group males at study week 4. The relationship to treatment for this change is uncertain, however, it was not considered adverse or toxicologically important because of the slight degree of change. There were no statistically significant changes in monocyte counts following the 4-week recovery period.

There were no other test substance-related effects on hematology parameters. However, some statistically significant differences were observed when the control and test substance-treated groups were compared. These findings included higher white blood cell counts, platelet counts and absolute lymphocyte counts and lower mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) in the 30 mg/kg/day group males on study week 8. These increases were not considered test substance-related because they occurred only at the recovery interval. Higher large unstained cell (LUC) counts in the 30 mg/kg/day group males at study week 4 were not considered toxicologically important. When microscopic correlations were done, the vast majority of LUC were lymphoid cells, so higher LUC counts are most likely a result of higher lymphocyte counts, also present in the 30 mg/kg/day group males at study week 4, although not statistically significant.

Statistically significant findings that involved percentage reticulocyte or leukocyte differential counts were not itemized above and were not considered toxicologically important because absolute cell counts are utilized for interpretative purposes.

2. Serum Chemistry

Summary Data: Tables 29, 30, 31, 32
Individual Data: Tables A23 through A30
Pathology Report: Appendix H

Test substance-related serum chemistry findings included changes in liver enzymes and serum proteins in males and females administered 3 and/or 30 mg/kg/day.

Liver enzyme levels (alanine aminotransferase [ALT], alkaline phosphatase [ALP] and sorbitol dehydrogenase [SDH]) were higher in the 3 and 30 mg/kg/day group males and 30 mg/kg/day group females at study week 4. Aspartate aminotransferase (AST) levels were also higher in the 3 and 30 mg/kg/day group males at study week 4. These liver enzyme level changes were consistent with hepatocellular injury (Solter, 2005) and single cell necrosis was noted microscopically in some animals in these groups. Liver enzyme changes were reversible in both males and females, as levels for all liver enzymes were similar to controls following 4 weeks of recovery. The only statistically significant change in liver enzymes in recovery group animals was a slight increase in SDH in the 30 mg/kg/day recovery group males. However, the group mean for this group was similar to that of the control group mean at the end of dosing, and there were no correlative changes in other liver enzymes and no microscopic changes in the livers of

animals in the 30 mg/kg/day recovery group males. Therefore, this slight increase in SDH was likely spurious and nonadverse. One animal in the 30 mg/kg/day recovery group males (no. 90941) had minimal increases in SDH and ALT, but the remaining liver enzymes were within the study control ranges. In addition, there were no microscopic changes in the liver of this animal. The basis of the slight increases in SDH and ALT in this animal was not determined.

Higher albumin, lower globulin, and associated changes of increased total protein and increased albumin/globulin ratio were present in the 30 mg/kg/day group males. Decreased globulin and increased albumin/globulin ratio were also present in the 3 mg/kg/day group males. A similar pattern of change in serum proteins was present in females administered 3 or 30 mg/kg/day. Decreases in acute phase proteins, which make up part of the serum globulin fraction are known to occur following treatment with other peroxisome proliferators (Gervois et al., 2004). Therefore, the changes in globulin were considered to be treatment related. However, individual globulin values in all affected groups were within or, in a few animals, slightly outside the WIL historical control range. Therefore, the changes in globulin were not considered to be adverse. Similarly, increased albumin, a negative acute phase protein, has also been reported following treatment with a peroxisome proliferator (Gervois et al., 2004). Therefore, the increases in albumin were also considered to be test substance-related. Except in the 30 mg/kg/day group males, individual values for albumin in most animals were within the WIL historical control range. In the 30 mg/kg/day group males, albumin values for most animals were above the WIL historical control range. However, there are no reported adverse biological effects associated with increased albumin. Therefore, changes in albumin were not considered to be adverse. The changes in albumin and globulin were reversible, as there were no statistically significant changes in these parameters in males or females by study week 8.

Blood urea nitrogen (BUN) was slightly increased in the 30 mg/kg/day group males at the end of exposure. The increase in urea nitrogen in 30 mg/kg/day group males was minimal, was not associated with correlative changes in serum creatinine or with test substance-related microscopic findings in the kidney, and thus was considered to be nonadverse. Blood urea nitrogen was similar to control values following the 4-week recovery period. Modest increases in BUN have been reported to occur following treatment with peroxisome proliferating compounds (Sheikh et al, 2006).

A statistically significant decrease in cholesterol was present in the 3 mg/kg/day group males. This decrease was not dose-related, as mean cholesterol in the 30 mg/kg/day group males was not statistically different from controls and was higher than that of the 3 mg/kg/day group males. However, several individual cholesterol values in treated group males were below the study control range, and thus, a test substance-related effect of decreased cholesterol can not be ruled out. However, individual cholesterol values in treated groups were within the WIL historical control range (with the exception of 1 male in the 3 mg/kg/day group) and thus changes in cholesterol were not considered to be adverse.

There were no other test substance-related effects on serum chemistry parameters. However, some statistically significant differences were observed when the control and test substance-treated groups were compared. These findings included slightly lower chloride levels

in the 30 mg/kg/day group males at study week 4; this slight decrease was not considered toxicologically important because of the small magnitude of change (-0.9%).

F. Anatomic Pathology

1. Macroscopic Examination

Summary Data: Tables 33, 34, 35, 36, 37

Individual Data: Tables A31, A32, A33, A34, A35

Pathology Report: Appendix H

Gross necropsy findings of enlarged liver, which correlates histologically with hepatocellular hypertrophy, were noted in the 30 mg/kg/day group males.

2. Organ Weights

Summary Data: Tables 38, 39, 40, 41

Individual Data: Tables A36 through A47

Pathology Report: Appendix H

There were no test substance-related alterations in final body weight.

Liver weights were increased in the 3 and 30 mg/kg/day group males and females at the end of the exposure period. These changes correlated with hepatocellular hypertrophy microscopically and with increases in beta-oxidation. Liver weight changes were mostly, but not completely, reversible in the 30 mg/kg/day group males and females. At this dose, liver weight relative to body weight in the 30 mg/kg/day group males was increased by 163.1% above controls at the end of exposure and was reduced to 21.5% of control after the 4-week recovery period.

Similarly, in 30 mg/kg/day group females, liver weight relative to body weight was increased by 102.7% above controls at the end of exposure and was reduced to 14.3% of control after the 4-week recovery period.

Adrenal gland weights (absolute and relative to body and brain weights) were increased in the 3 and 30 mg/kg/day group males at the end of the exposure period. In the 30 mg/kg/day group males, these adrenal weight changes correlated with minimal adrenal cortical hypertrophy microscopically. Adrenal weight changes were reversible following the 4-week recovery period.

Decreased uterus weights (absolute and relative to body and brain weights) were present in the 30 mg/kg/day females at the end of the exposure period. There were no histopathological changes in the uterus that were correlative to the uterine weight changes. However, more animals in the 30 mg/kg/day group were in diestrus (based on vaginal histology) compared to controls (see discussion under Microscopic Examination), and uterine weights are typically less during diestrus compared to estrus or proestrus. In the recovery groups, uterine weights were similar among treated and control groups.

There were no other test substance-related effects on organ weights. However, some statistically significant differences were observed when the control and test substance-treated groups were

compared. At the primary necropsy, there were higher mean absolute kidneys weights in the 0.1 (\uparrow 11.0%) and 30 (\uparrow 20.6%) mg/kg/day group females, higher mean kidney weights relative to final body weight in the 0.1 (\uparrow 8.3%) and 30 (\uparrow 17.4%) mg/kg/day group females, and higher mean kidneys weight relative to brain weight in the 30 (\uparrow 19.1%) mg/kg/day group females. At the primary necropsy, there were higher mean absolute spleen weight (\uparrow 27.3%) and mean spleen weight relative to final body weight (\uparrow 23.6%) in the 0.1 mg/kg/day group females. The absolute weights and weights relative to body or brain weight were discordant or the dose association was incoherent; thus these organ weight changes were considered to be spurious. At the recovery necropsy, there were higher mean absolute adrenal glands weight (\uparrow 21.0%) and higher mean adrenal glands weight relative to brain weight (\uparrow 20.9%) in the 30 mg/kg/day group females. The individual animal adrenal gland weights for the 30 mg/kg/day recovery group females were similar to the individual animal adrenal gland weights for the primary control group females, and there were no gross or histologic correlates to the adrenal gland weight changes; thus these organ weight changes were considered to be spurious.

3. Microscopic Examination

Summary Data: Tables 42, 43, 44, 45, 46

Individual Data: Tables A31, A32, A33, A34, A35

Pathology Report: Appendix H

Minimal adrenal cortical hypertrophy was observed in the 30 mg/kg/day group males at the primary necropsy. This change correlated with increased adrenal weights in this group. Adrenal cortical hypertrophy was not observed in the 30 mg/kg/day group males at the recovery necropsy.

Hepatocellular hypertrophy was observed in the 3 and 30 mg/kg/day group males and females at the primary necropsy. This change was consistent with increased liver weights noted in these groups. The hepatocellular hypertrophy was characterized by expansion of the hepatocellular cytoplasm by numerous fine eosinophilic granules lending a generalized eosinophilic tinctorial change to the affected livers. The distribution of the hepatocellular hypertrophy was centrilobular when of minimal or mild severity and diffuse when of moderate severity. In addition, there was multifocal single cell hepatocellular necrosis in the 3 and 30 mg/kg/day group males and 30 mg/kg/day group females at the primary necropsy, and increased mitoses distributed multifocally throughout the liver section in the 30 mg/kg/day group males and females at the primary necropsy. Incidences of the changes were higher in the males compared to the females. Hepatocellular hypertrophy, single cell hepatocellular necrosis and increased mitoses in the liver were not observed in the 30 mg/kg/day group males and females at the recovery necropsy.

There was an increased number of animals in the diestrus stage of the estrous cycle in the 30 mg/kg/day group females compared to control group females at the primary necropsy. While this finding could be indicative of potential effects on the estrous cycle, ovarian morphology, including number and maturational stages of corpora lutea were similar between treated and control groups, suggesting normal estrous cycling. Therefore, the significance of the differences in estrous stage distribution between the 30 mg/kg/day group females and control group females

is uncertain. The number of animals in the diestrus stage of the estrous cycle was equal in the control and 30 mg/kg/day group females at the recovery necropsy.

At the primary necropsy, subacute inflammation in the region of the aorta, esophagus, pharynx, and/or thymus was observed in 1 control group male (no. 90953), one 30 mg/kg/day group male (no. 90902), 1 control group female (no. 90995), and three 30 mg/kg/day group females (nos. 90983, 91026, and 91040); necrosis and neutrophilic infiltration in the region of the thymus was observed in 1 control group female (no. 91018). These histologic findings were consistent with gavage injuries.

At the recovery necropsy, pyogranulomatous inflammation and foreign material were observed in the adipose tissue and bronchial lymph node of 1 control group female (no. 90984) and in the region of the esophagus, mammary gland and skin in one 30 mg/kg/day group female (no. 91007). Reactive plasmacytosis was identified in the bronchial, mandibular, and/or mediastinal lymph nodes in these 2 animals. These histologic findings could be consistent with gavage injuries or other traumatic injury introducing foreign material into the tissues with subsequent pyogranulomatous inflammation.

There were no other test substance-related histologic changes. Remaining histologic changes were considered to be incidental findings or related to some aspect of experimental manipulation other than administration of the test substance. There was no test substance-related alteration in the prevalence, severity or histologic character of those incidental tissue alterations.

G. Liver Metabolic Enzyme Analyses

Liver Metabolic Enzyme Analyses: Appendix I

In male mice at the 28-day time point, beta-oxidation activity was statistically significantly increased at dosage levels of 0.1, 3 and 30 mg/kg/day H-28397. Beta-oxidation was increased about 8-fold above control in the 3 and 30 mg/kg/day group males, with minimal increases of about 1.5-fold in 0.1 mg/kg/day group males. Total cytochrome P-450 content was statistically significantly decreased in males at a dosage of 3 and 30 mg/kg/day H-28397 (26 and 44% below the control group, respectively). Beta-oxidation activity returned to the control level at the 28-day recovery time point. Total cytochrome P-450 content remained decreased at 30 mg/kg/day H-28397 (88% of the control group) after approximately 28 days of recovery.

In female mice at the 28-day time point, beta-oxidation activity was statistically significantly increased at dosages of 3 and 30 mg/kg/day H-28397 (increases were about 6- and 9-fold higher than the control group, respectively). No alteration in total cytochrome P-450 content was observed. Beta-oxidation activity returned to the control level at the 28-day recovery time point.

CONCLUSIONS

Based on the results of this study, H-28397 administered orally (gavage) to Crl:CD1(ICR) mice at dosage levels of 0.1, 3 and 30 mg/kg/day for 28 consecutive days was well tolerated. Most test substance-related effects were consistent with a peroxisome proliferator (PPAR α agonist) and included increased beta-oxidation in the liver, increased liver weights, hepatocellular hypertrophy, and changes in serum lipids and proteins. Other changes included increased body weights, minimal decreases in red cell mass parameters and increased adrenal weights and adrenal cortical hypertrophy. These effects were reversible following a 4-week recovery period. Adverse effects were noted in the liver of males at 3 mg/kg/day and above and females at 30 mg/kg/day. These consisted of single cell necrosis of hepatocytes and correlative increases in liver enzymes. These effects were also reversible following the 4-week recovery period. Therefore, the no-observed-adverse-effect level (NOAEL) for oral (gavage) administration of H-28397 to Crl:CD1(ICR) mice for 28 consecutive days was 0.1 mg/kg/day for males and 3 mg/kg/day in females.

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DEVIATIONS FROM THE PROTOCOL

This study was conducted in accordance with the protocol and protocol amendments, except for the following.

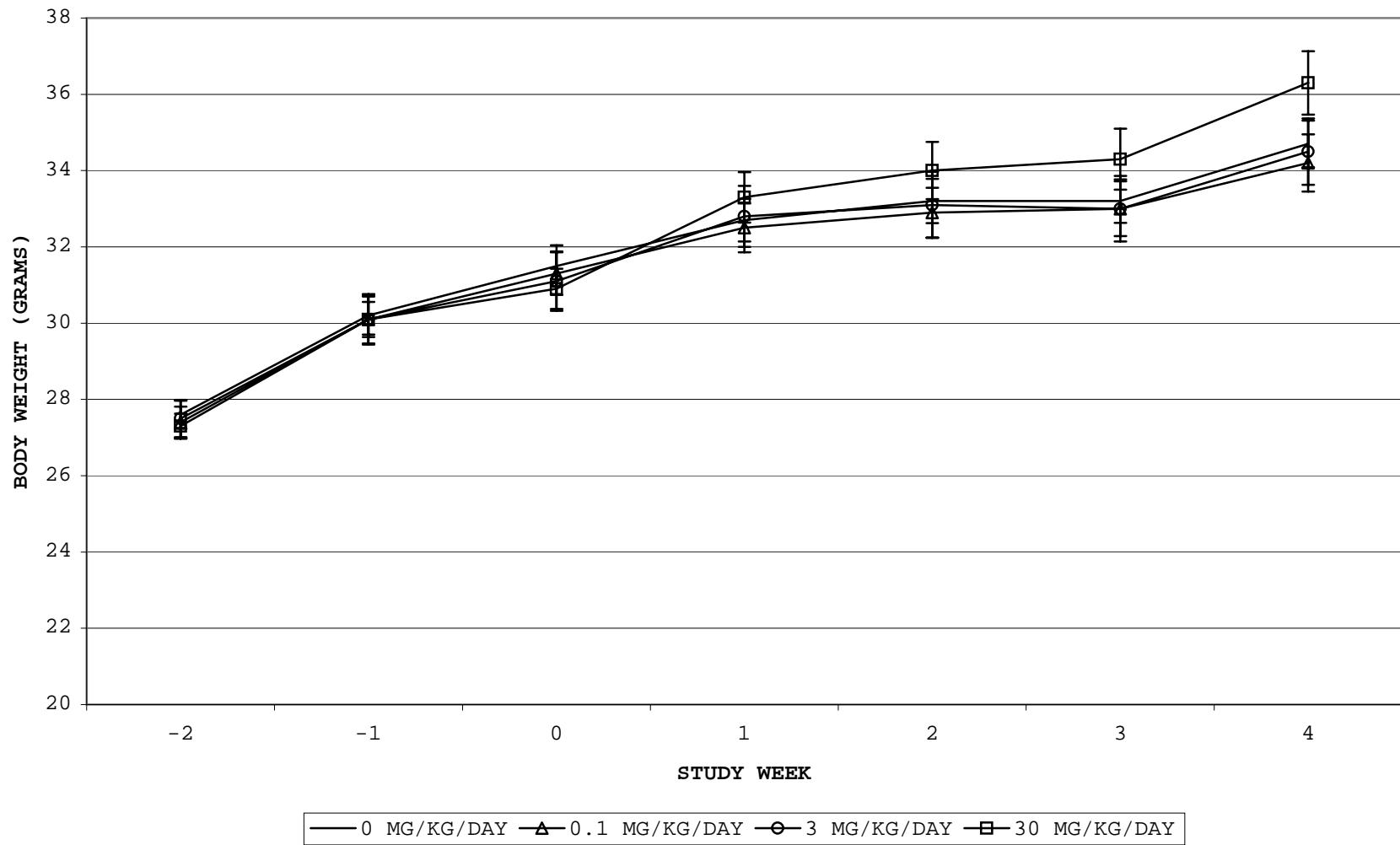
- **Protocol Section 7.4.5** states that dose levels are to become effective on the day new body weights are recorded. On 8 January 2008 (study day 21), the body weights from the previous weighing were used for dose administration to all Group 1 males (0 mg/kg/day).
- **Protocol Section 8.7.1** states that the pancreas, duodenum, jejunum, ileum, cecum, colon and mesenteric lymph nodes are to be collected and placed in 10% neutral buffered formalin. According to SOP T3-030-12, specimens are to be placed into a 10% neutral buffered formalin-filled container that is labeled to include the study number, animal number and fixative. On 16 January 2008, 2 of each of the organs listed above were present in the formalin-filled jar for female no. 91037 (Group 1, 0 mg/kg/day). These same tissues were missing from the formalin-filled jar for female no. 91027 (Group 4, 30 mg/kg/day). Both sets of tissues remained in the jar for female no. 91037.
- **Protocol Section 8.7.1** states that the left and median lobes of the liver are to be retained at the time of necropsy. On 16 January 2008, the left lobe of the liver of female no. 91002 (Group 1, 0 mg/kg/day) was not present. No histological processing was performed on the tissue section.
- **Protocol Section 8.6** states that blood samples for serum chemistry and hematology will be collected from the retro-orbital sinus of animals anesthetized by inhalation of isoflurane, and that in the event that sufficient blood can be collected to perform both analyses priority will be given to serum chemistry. On 16 January 2008 (study day 28), after serum chemistry analyses had been performed, it was discovered that calcium levels had not been evaluated for female no. 91004 (Group 4, 30 mg/kg/day). Because an insufficient amount of serum remained for calcium evaluation, the calcium entry for this animal in the data tables was entered as QNS (quantity not sufficient). In addition, phosphorous analyses were not performed in accordance with the order of priority for female nos. 91037 (Group 1, 0 mg/kg/day), 90988 (Group 3, 3 mg/kg/day) and 91002 (Group 1, 0 mg/kg/day).
- **Protocol Section 8.7.3** states that a section of the liver from each animal is to be frozen in a plastic bag. The liver sections were collected and placed in cryovials.

These deviations did not negatively impact the quality or integrity of the data nor the outcome of the study.

FIGURES 1 - 4

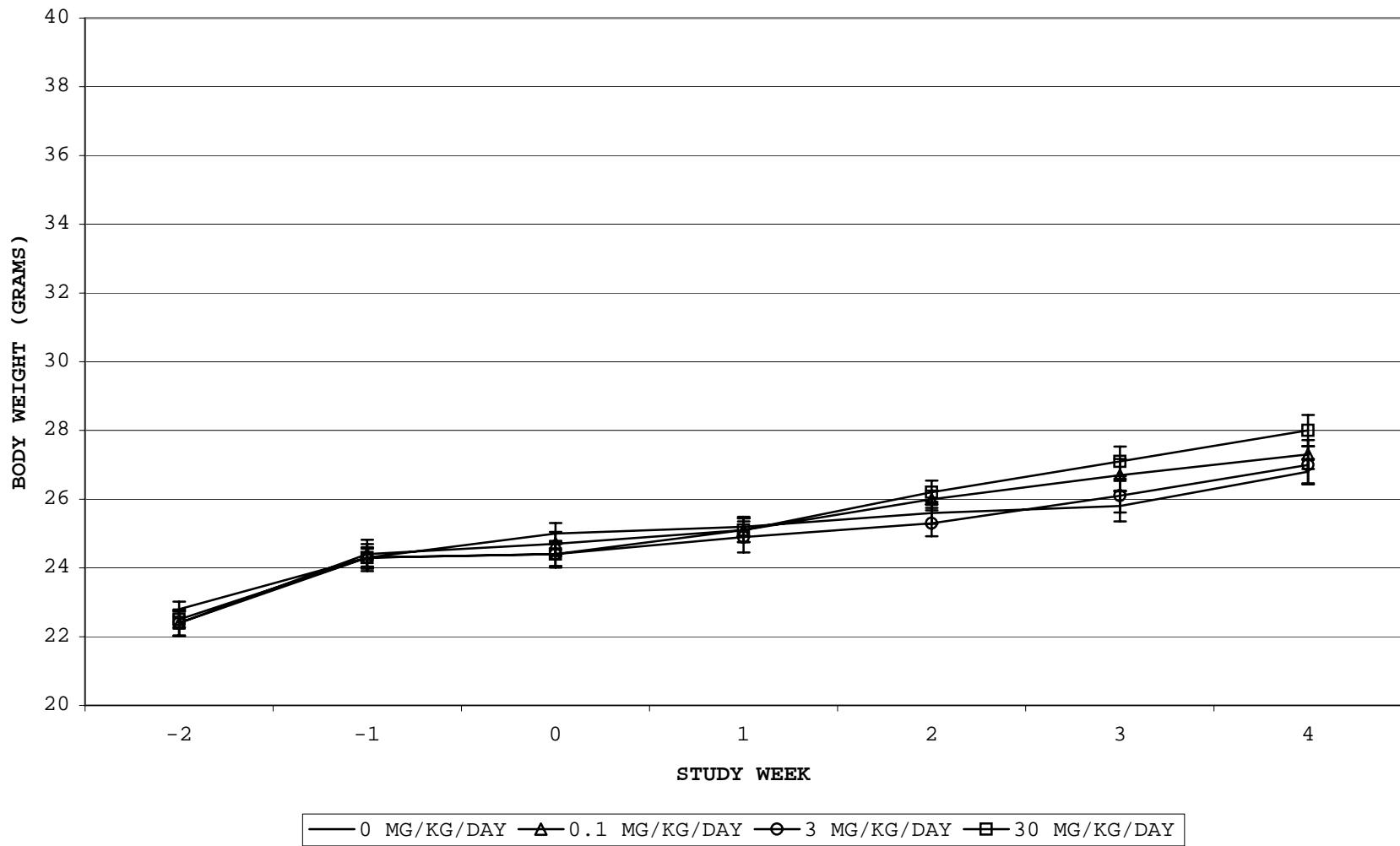
PROJECT NO.:WIL-189207
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SPONSOR NO.:DUPONT-24459

FIGURE 1
SUMMARY OF BODY WEIGHTS (G) - DOSING PERIOD - MALES



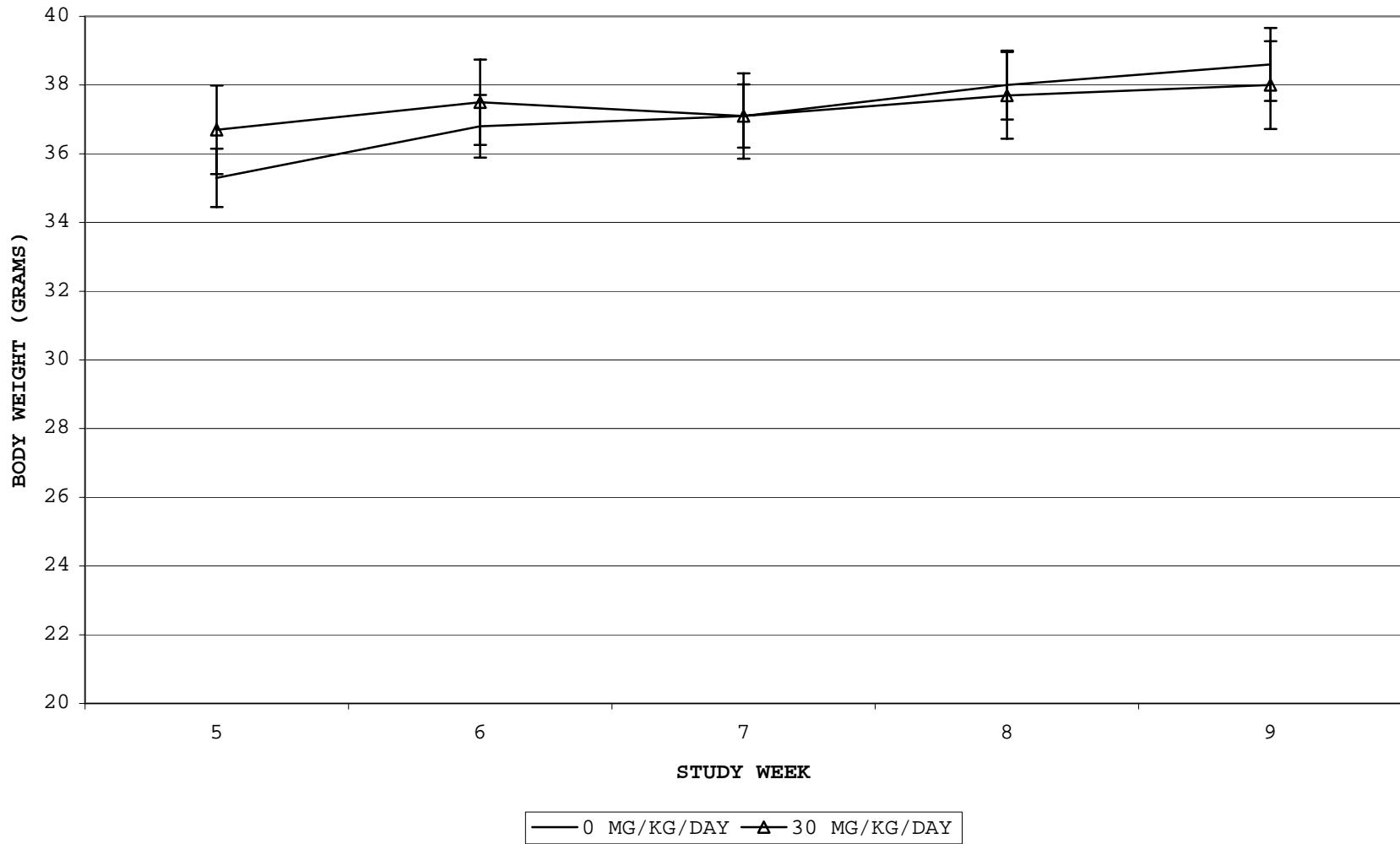
PROJECT NO.:WIL-189207
SPONSOR:E.I. DUPONT
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FIGURE 2
SUMMARY OF BODY WEIGHTS (G) - DOSING PERIOD - FEMALES



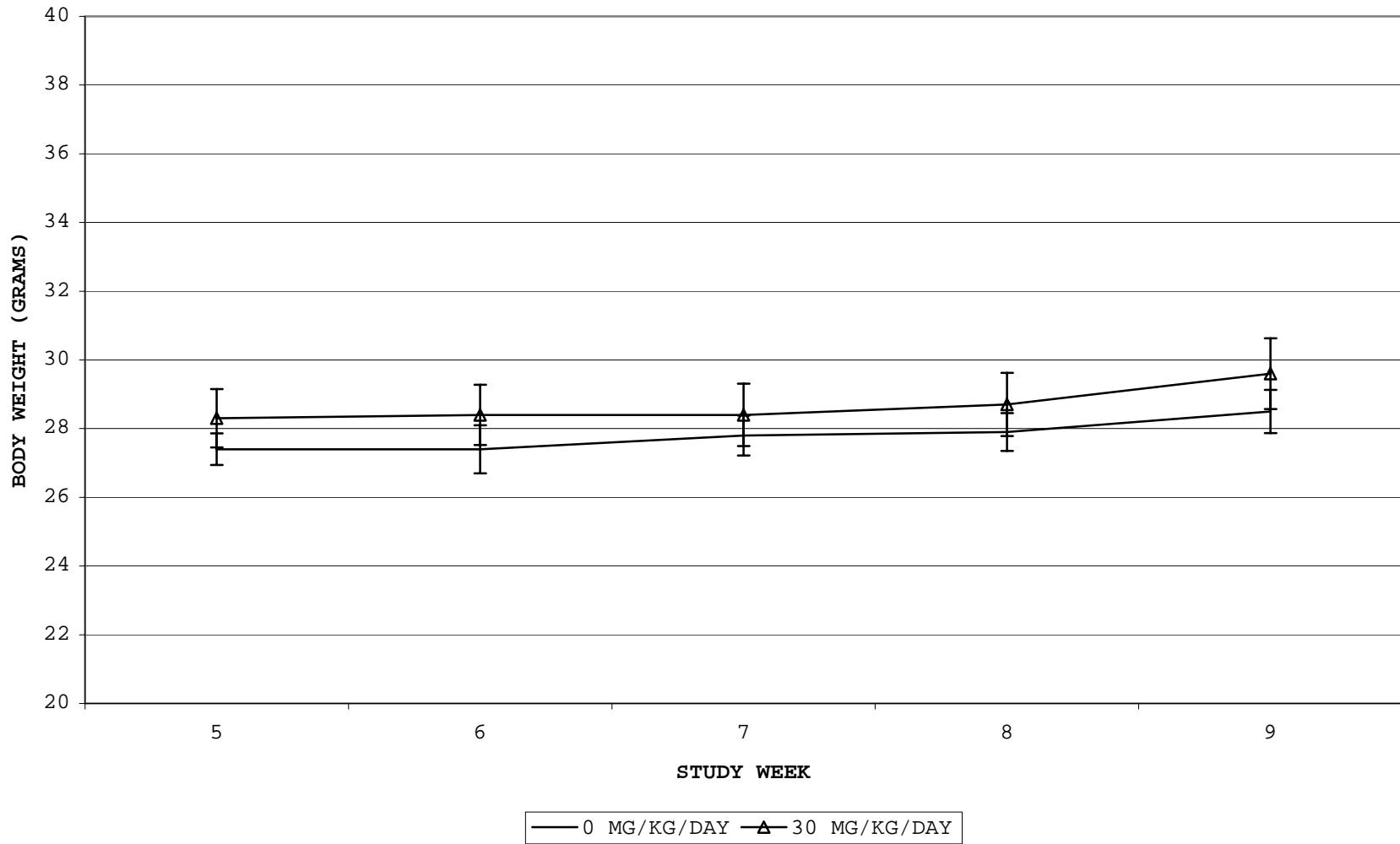
PROJECT NO.:WIL-189207
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FIGURE 3
SUMMARY OF BODY WEIGHTS (G) - RECOVERY PERIOD - MALES



PROJECT NO.:WIL-189207
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FIGURE 4
SUMMARY OF BODY WEIGHTS (G) - RECOVERY PERIOD - FEMALES



TABLES 1 - 46

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
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TABLE 1 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SURVIVAL AND DISPOSITION

PAGE 1

GROUP :	1				2				3				4			
	LIVE	FD	EE	SE												
0	20	0	0	0	10	0	0	0	10	0	0	0	20	0	0	0
1	20	0	0	0	10	0	0	0	10	0	0	0	20	0	0	0
2	20	0	0	0	10	0	0	0	10	0	0	0	20	0	0	0
3	20	0	0	0	10	0	0	0	10	0	0	0	20	0	0	0
4	10	0	0	10	0	0	0	10	0	0	0	10	10	0	0	10
5	10	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0
6	10	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0
7	10	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0
8	0	0	0	10	0	0	0	0	0	0	0	0	0	0	0	10

WEEK = WEEK OF STUDY FD = FOUND DEAD EE = EUTHANIZED IN EXTREMIS SE = SCHEDULED EUTHANASIA

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 2 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SURVIVAL AND DISPOSITION

PAGE 1

GROUP :	1				2				3				4			
	LIVE	FD	EE	SE												
0	20	0	0	0	10	0	0	0	10	0	0	0	20	0	0	0
1	20	0	0	0	10	0	0	0	10	0	0	0	19	1	0	0
2	20	0	0	0	10	0	0	0	10	0	0	0	19	0	0	0
3	19	1	0	0	10	0	0	0	10	0	0	0	19	0	0	0
4	9	0	0	10	0	0	0	10	0	0	0	10	9	0	0	10
5	9	0	0	0	0	0	0	0	0	0	0	0	9	0	0	0
6	9	0	0	0	0	0	0	0	0	0	0	0	9	0	0	0
7	9	0	0	0	0	0	0	0	0	0	0	0	9	0	0	0
8	0	0	0	9	0	0	0	0	0	0	0	0	0	0	0	9

WEEK = WEEK OF STUDY FD = FOUND DEAD EE = EUTHANIZED IN EXTREMIS SE = SCHEDULED EUTHANASIA

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

PSURVV4.09
04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - DOSING PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PAGE 1

----- M A L E -----

TABLE RANGE: GROUP:	DAY 000 TO DAY 028			
	1	2	3	4
NORMAL				
-NO SIGNIFICANT CLINICAL OBSERVATIONS	98/20	45/10	42/10	91/20
DISPOSITION				
-PRIMARY NECROPSY (DAY 28)	10/10	10/10	10/10	10/10
EYES/EARS/NOSE				
-OPACITY RIGHT EYE	0/ 0	1/ 1	0/ 0	0/ 0
-ABNORMAL PUPIL POSITION LEFT EYE	1/ 1	1/ 1	5/ 2	6/ 3
-ABNORMAL PUPIL POSITION RIGHT EYE	0/ 0	3/ 1	3/ 1	4/ 1
BODY/INTEG II				
-SCABBING MEDIAL TAIL	1/ 1	0/ 0	0/ 0	0/ 0
ORAL/DENTAL				
-WET RED MATERIAL AROUND MOUTH	0/ 0	0/ 0	0/ 0	1/ 1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

TABLE 4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - DOSING PERIOD - FEMALES)
 PROJECT NO.: WIL-189207F
 SPONSOR: E.I. DUPONT
 SPONSOR NO.: DUPONT-24459

PAGE 1

SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

TABLE RANGE: GROUP:	1	DAY 000 TO DAY 028	2	3	4
NORMAL					
-NO SIGNIFICANT CLINICAL OBSERVATIONS	82/20		48/10	44/10	94/20
DISPOSITION					
-FOUND DEAD	1/ 1		0/ 0	0/ 0	1/ 1
-PRIMARY NECROPSY (DAY 28)	10/10		10/10	10/10	10/10
BODY/INTEGUMENT					
-HAIR LOSS FORELIMB(S)	0/ 0		0/ 0	2/ 2	0/ 0
-DERMAL ATONIA	1/ 1		0/ 0	0/ 0	0/ 0
-THIN	1/ 1		0/ 0	0/ 0	0/ 0
EYES/EARS/NOSE					
-ABNORMAL PUPIL POSITION LEFT EYE	0/ 0		1/ 1	0/ 0	0/ 0
-ABNORMAL PUPIL POSITION RIGHT EYE	11/ 3		0/ 0	0/ 0	0/ 0
-WET RED MATERIAL AROUND NOSE	1/ 1		0/ 0	0/ 0	0/ 0
EXCRETA					
-DEFECATION DECREASED	1/ 1		0/ 0	0/ 0	0/ 0
-FECES SMALLER THAN NORMAL	1/ 1		0/ 0	0/ 0	0/ 0
BODY/INTEG II					
-SCABBING MEDIAL TAIL	0/ 0		0/ 0	0/ 0	1/ 1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - DOSING PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PAGE 2

----- F E M A L E -----

TABLE RANGE: GROUP:	DAY 000 TO DAY 028			
	1	2	3	4
BODY/INTEG II				
-SCABBING END OF TAIL	1/ 1	0/ 0	3/ 1	0/ 0
-SCABBING RIGHT EAR	2/ 2	1/ 1	1/ 1	1/ 1
ORAL/DENTAL				
-UPPER INCISOR(S) MISSING	1/ 1	0/ 0	0/ 0	0/ 0
SPECIAL				
-SWOLLEN FACIAL AREA	0/ 0	0/ 0	0/ 0	1/ 1
SPECIAL II				
-DIGIT(S) MISSING LEFT FORELIMB	1/ 1	0/ 0	0/ 0	0/ 0

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

TABLE 5 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - RECOVERY PERIOD - MALES)
 PROJECT NO.: WIL-189207M A 28-DAY ORAL STUDY OF H-28397 IN MICE
 SPONSOR: E.I. DUPONT SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS
 SPONSOR NO.: DUPONT-24459

PAGE 1

----- M A L E -----

TABLE RANGE: GROUP:	DAY 029 TO DAY 058			
	1	2	3	4
NORMAL				
-NO SIGNIFICANT CLINICAL OBSERVATIONS	35 / 9	0 / 0	0 / 0	39 / 10
DISPOSITION				
-RECOVERY NECROPSY (WEEK 8)	10 / 10	0 / 0	0 / 0	10 / 10
EYES/EARS/NOSE				
-ABNORMAL PUPIL POSITION LEFT EYE	4 / 1	0 / 0	0 / 0	0 / 0
BODY/INTEG III				
-WET YELLOW MATERIAL UROGENITAL AREA	1 / 1	0 / 0	0 / 0	0 / 0
SPECIAL II				
-TAIL BROKEN	0 / 0	0 / 0	0 / 0	1 / 1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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04/21/2008
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TABLE 6 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - RECOVERY PERIOD - FEMALES)
 PROJECT NO.: WIL-189207F
 SPONSOR: E.I. DUPONT
 SPONSOR NO.: DUPONT-24459

PAGE 1

A 28-DAY ORAL STUDY OF H-28397 IN MICE
 SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

TABLE RANGE: GROUP:	1	DAY 029 TO DAY 057 2	3	4
NORMAL				
-NO SIGNIFICANT CLINICAL OBSERVATIONS	27 / 8	0 / 0	0 / 0	32 / 8
DISPOSITION				
-RECOVERY NECROPSY (WEEK 8)	9 / 9	0 / 0	0 / 0	9 / 9
BEHAVIOR/CNS				
-PARTIAL CLOSURE RIGHT EYE	0 / 0	0 / 0	0 / 0	1 / 1
EYES/EARS/NOSE				
-ABNORMAL PUPIL POSITION RIGHT EYE	8 / 3	0 / 0	0 / 0	0 / 0
-PURULENT DISCHARGE RIGHT EYE	0 / 0	0 / 0	0 / 0	1 / 1
BODY/INTEG II				
-SCABBING FACIAL AREA	0 / 0	0 / 0	0 / 0	1 / 1
SPECIAL II				
-TAIL BROKEN	1 / 1	0 / 0	0 / 0	0 / 0
-MASS, DORSAL TRUNK, 35MM X 17MM X 5MM, SMOOTH, SOFT, IMMOVABLE, NORMAL SURFACE	0 / 0	0 / 0	0 / 0	2 / 1
-MASS, DORSAL HEAD, 5MM X 5MM X 5MM, SMOOTH, FIRM, IMMOVABLE, SCABBED, DISCOLORED	0 / 0	0 / 0	0 / 0	2 / 1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

TABLE 6 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - RECOVERY PERIOD - FEMALES)
PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

PAGE 2

A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

TABLE RANGE: GROUP:	1	DAY 029 TO DAY 057	2	3	4
SPECIAL II					
-MASS, FACIAL AREA, 4MM X 5MM X 3MM, SMOOTH, FIRM, IMMOVABLE, SCABBED, DISCOLORED	0 / 0		0 / 0		2 / 1
-MASS, FACIAL AREA, 4MM X 3MM X 2MM, SMOOTH, FIRM, IMMOVABLE, SCABBED, DISCOLORED	0 / 0		0 / 0		1 / 1
-MASS, DORSAL NECK, 30MM X 15MM X 12MM, NODULAR, FIRM, MOVABLE, NORMAL SURFACE	0 / 0		0 / 0		1 / 1
-MASS, DORSAL NECK, 35MM X 17MM X 10MM, SMOOTH, FIRM, IMMOVABLE, NORMAL SURFACE	0 / 0		0 / 0		1 / 1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 7 (DOSING DAY OBSERVATIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF POST-DOSE FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PAGE 1

----- M A L E -----

TABLE RANGE:	DAY 0 TO DAY 27			
	GROUP: 1	2	3	4

NORMAL

TIME OF DOSE

-NO SIGNIFICANT CLINICAL OBSERVATIONS 556/20 278/10 280/10 556/20

APPROX. 1-2 HOURS POST-DOSE

-NO SIGNIFICANT CLINICAL OBSERVATIONS 556/20 272/10 275/10 555/20

EYES/EARS/NOSE

TIME OF DOSE

-DRIED RED MATERIAL AROUND NOSE 0/0 0/0 0/0 1/1

BODY/INTEG III

TIME OF DOSE

-WET YELLOW MATERIAL UROGENITAL AREA	4/4	0/0	0/0	1/1
-DRIED YELLOW MATERIAL UROGENITAL AREA	0/0	2/1	0/0	2/2

APPROX. 1-2 HOURS POST-DOSE

-WET YELLOW MATERIAL UROGENITAL AREA	3/2	1/1	5/4	2/2
-WET YELLOW MATERIAL ANOGENITAL AREA	0/0	0/0	1/1	0/0
-DRIED YELLOW MATERIAL UROGENITAL AREA	1/1	7/2	0/0	3/2
-DRIED YELLOW MATERIAL VENTRAL TRUNK	0/0	0/0	0/0	1/1
-DRIED YELLOW MATERIAL ANOGENITAL AREA	0/0	0/0	0/0	1/1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 8 (DOSING DAY OBSERVATIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF POST-DOSE FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PAGE 1

----- F E M A L E -----

TABLE RANGE:	DAY 0 TO DAY 27			
	GROUP: 1	2	3	4

NORMAL

TIME OF DOSE

-NO SIGNIFICANT CLINICAL OBSERVATIONS 553/20 279/10 280/10 535/20

APPROX. 1-2 HOURS POST-DOSE

-NO SIGNIFICANT CLINICAL OBSERVATIONS 555/20 280/10 280/10 535/20

BODY/INTEGUMENT

TIME OF DOSE

-DERMAL ATONIA 3/1 0/0 0/0 0/0

-THIN

1/1 0/0 0/0 0/0

APPROX. 1-2 HOURS POST-DOSE

-DERMAL ATONIA 1/1 0/0 0/0 0/0

EYES/EARS/NOSE

APPROX. 1-2 HOURS POST-DOSE

-WET RED MATERIAL AROUND NOSE 1/1 0/0 0/0 0/0

EXCRETA

TIME OF DOSE

-DEFECATION DECREASED 4/1 0/0 0/0 0/0

-FECES SMALLER THAN NORMAL 2/1 0/0 0/0 0/0

APPROX. 1-2 HOURS POST-DOSE

-DEFECATION DECREASED 0/0 0/0 0/0 2/1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 8 (DOSING DAY OBSERVATIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF POST-DOSE FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PAGE 2

----- F E M A L E -----

TABLE RANGE: GROUP:	DAY 0 TO DAY 27			
	1	2	3	4

SPECIAL

TIME OF DOSE

-SWOLLEN FACIAL AREA	0/0	0/0	0/0	2/1
-SWOLLEN LEFT FORELIMB	0/0	0/0	0/0	1/1
-SWOLLEN RIGHT FORELIMB	0/0	0/0	0/0	2/1

APPROX. 1-2 HOURS POST-DOSE

-SWOLLEN FACIAL AREA	0/0	0/0	0/0	1/1
-SWOLLEN RIGHT FORELIMB	0/0	0/0	0/0	2/1

BODY/INTEG III

TIME OF DOSE

-WET YELLOW MATERIAL UROGENITAL AREA	0/0	1/1	0/0	2/1
-WET YELLOW MATERIAL VENTRAL TRUNK	0/0	0/0	0/0	1/1
-DRIED YELLOW MATERIAL UROGENITAL AREA	1/1	0/0	0/0	0/0

APPROX. 1-2 HOURS POST-DOSE

-WET YELLOW MATERIAL UROGENITAL AREA	0/0	0/0	0/0	1/1
-DRIED YELLOW MATERIAL UROGENITAL AREA	1/1	0/0	0/0	0/0

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207H
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 9 (DAILY OBSERVATIONS - RECOVERY PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PAGE 1

----- M A L E -----

TABLE RANGE: GROUP:	DAY 029 TO DAY 057			
	1	2	3	4
NORMAL				
-NO SIGNIFICANT CLINICAL OBSERVATIONS	258/10	0 / 0	0 / 0	260/10
BODY/INTEG III				
-WET YELLOW MATERIAL UROGENITAL AREA	2 / 1	0 / 0	0 / 0	0 / 0
-DRIED YELLOW MATERIAL UROGENITAL AREA	1 / 1	0 / 0	0 / 0	0 / 0

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207W
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 10 (DAILY OBSERVATIONS - RECOVERY PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PAGE 1

----- F E M A L E -----

TABLE RANGE: GROUP:	DAY 029 TO DAY 056			
	1	2	3	4
NORMAL				
-NO SIGNIFICANT CLINICAL OBSERVATIONS	224 / 9	0 / 0	0 / 0	205 / 9
SPECIAL				
-SWOLLEN FACIAL AREA	0 / 0	0 / 0	0 / 0	18 / 1
BODY/INTEG III				
-WET YELLOW MATERIAL VENTRAL TRUNK	1 / 1	0 / 0	0 / 0	0 / 0
SPECIAL II				
-SWOLLEN DORSAL NECK	0 / 0	0 / 0	0 / 0	15 / 1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 11 (DOSING PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHTS [G]

PAGE 1

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
WEEK -2				
MEAN	27.6	27.4	27.5	27.3
% DIFFERENCE		-0.7	-0.4	-1.1
S.D.	1.67	1.29	1.54	1.50
S.E.	0.37	0.41	0.49	0.33
N	20	10	10	20
-1				
MEAN	30.2	30.1	30.1	30.1
% DIFFERENCE		-0.3	-0.3	-0.3
S.D.	2.24	2.00	2.09	2.07
S.E.	0.50	0.63	0.66	0.46
N	20	10	10	20
0				
MEAN	31.5	31.3	31.1	30.9
% DIFFERENCE		-0.6	-1.3	-1.9
S.D.	2.39	1.76	2.46	2.36
S.E.	0.54	0.56	0.78	0.53
N	20	10	10	20
1				
MEAN	32.7	32.5	32.8	33.3
% DIFFERENCE		-0.6	0.3	1.8
S.D.	2.51	2.02	2.55	2.94
S.E.	0.56	0.64	0.80	0.66
N	20	10	10	20

None significantly different from control group

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 11 (DOSING PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHTS [G]

PAGE 2

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
WEEK 2				
MEAN	33.2	32.9	33.1	34.0
% DIFFERENCE		-0.9	-0.3	2.4
S.D.	2.59	2.05	2.75	3.36
S.E.	0.58	0.65	0.87	0.75
N	20	10	10	20
3				
MEAN	33.2	33.0	33.0	34.3
% DIFFERENCE		-0.6	-0.6	3.3
S.D.	2.56	2.28	2.71	3.58
S.E.	0.57	0.72	0.86	0.80
N	20	10	10	20
4				
MEAN	34.7	34.2	34.5	36.3
% DIFFERENCE		-1.4	-0.6	4.6
S.D.	2.74	2.38	2.75	3.70
S.E.	0.61	0.75	0.87	0.83
N	20	10	10	20

None significantly different from control group

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 12 (DOSING PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHTS [G]

PAGE 1

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
WEEK -2				
MEAN	22.8	22.4	22.4	22.5
% DIFFERENCE		-1.8	-1.8	-1.3
S.D.	0.99	1.15	1.23	1.03
S.E.	0.22	0.36	0.39	0.23
N	20	10	10	20
-1				
MEAN	24.3	24.4	24.3	24.3
% DIFFERENCE		0.4	0.0	0.0
S.D.	1.18	1.32	1.24	1.35
S.E.	0.26	0.42	0.39	0.30
N	20	10	10	20
0				
MEAN	25.0	24.7	24.4	24.4
% DIFFERENCE		-1.2	-2.4	-2.4
S.D.	1.40	1.12	1.23	1.53
S.E.	0.31	0.35	0.39	0.34
N	20	10	10	20
1				
MEAN	25.2	25.1	24.9	25.1
% DIFFERENCE		-0.4	-1.2	-0.4
S.D.	1.29	1.06	1.42	1.56
S.E.	0.29	0.34	0.45	0.35
N	20	10	10	20

None significantly different from control group

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 12 (DOSING PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHTS [G]

PAGE 2

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
WEEK 2				
MEAN	25.6	26.0	25.3	26.2
% DIFFERENCE		1.6	-1.2	2.3
S.D.	1.43	0.78	1.19	1.47
S.E.	0.32	0.25	0.38	0.34
N	20	10	10	19
3				
MEAN	25.8	26.7	26.1	27.1
% DIFFERENCE		3.5	1.2	5.0
S.D.	2.02	1.47	1.56	1.86
S.E.	0.45	0.47	0.49	0.43
N	20	10	10	19
4				
MEAN	26.8	27.3	27.0	28.0
% DIFFERENCE		1.9	0.7	4.5
S.D.	1.60	1.32	1.70	1.98
S.E.	0.37	0.42	0.54	0.45
N	19	10	10	19

None significantly different from control group

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 13 (RECOVERY PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHTS [G]

PAGE 1

GROUP:	MALES				
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY	
WEEK 5					
MEAN	35.3	NA	NA	36.7	
% DIFFERENCE				4.0	
S.D.	2.68			4.08	
S.E.	0.85			1.29	
N	10			10	
6					
MEAN	36.8	NA	NA	37.5	
% DIFFERENCE				1.9	
S.D.	2.89			3.93	
S.E.	0.91			1.24	
N	10			10	
7					
MEAN	37.1	NA	NA	37.1	
% DIFFERENCE				0.0	
S.D.	2.90			3.91	
S.E.	0.92			1.24	
N	10			10	
8					
MEAN	38.0	NA	NA	37.7	
% DIFFERENCE				-0.8	
S.D.	3.17			3.99	
S.E.	1.00			1.26	
N	10			10	

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 13 (RECOVERY PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHTS [G]

PAGE 2

GROUP:	MALES			PAGE
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	
WEEK 9				
MEAN	38.6	NA	NA	38.0
% DIFFERENCE				-1.6
S.D.	3.36			4.04
S.E.	1.06			1.28
N	10			10

None significantly different from control group
NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

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PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
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TABLE 14 (RECOVERY PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHTS [G]

PAGE 1

GROUP:	FEMALES				
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY	
WEEK 5					
MEAN	27.4	NA	NA	28.3	
% DIFFERENCE				3.3	
S.D.	1.38			2.54	
S.E.	0.46			0.85	
N	9			9	
6					
MEAN	27.4	NA	NA	28.4	
% DIFFERENCE				3.6	
S.D.	2.11			2.63	
S.E.	0.70			0.88	
N	9			9	
7					
MEAN	27.8	NA	NA	28.4	
% DIFFERENCE				2.2	
S.D.	1.75			2.74	
S.E.	0.58			0.91	
N	9			9	
8					
MEAN	27.9	NA	NA	28.7	
% DIFFERENCE				2.9	
S.D.	1.66			2.76	
S.E.	0.55			0.92	
N	9			9	

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 14 (RECOVERY PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHTS [G]

PAGE 2

GROUP:	FEMALES			PAGE	2
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY		
WEEK 9					
MEAN	28.5	NA	NA	29.6	
% DIFFERENCE				3.9	
S.D.	1.90			3.10	
S.E.	0.63			1.03	
N	9			9	

None significantly different from control group
NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 15 (DOSING PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHT CHANGES [G]

PAGE 1

WEEK	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
-2 TO -1	MEAN	2.6	2.7	2.6	2.8
	S.D.	0.76	1.32	1.07	1.06
	S.E.	0.17	0.42	0.34	0.24
	N	20	10	10	20
-1 TO 0	MEAN	1.4	1.2	1.0	0.7**
	S.D.	0.54	0.59	0.68	0.62
	S.E.	0.12	0.19	0.21	0.14
	N	20	10	10	20
0 TO 1	MEAN	1.1	1.3	1.7	2.5**
	S.D.	0.74	0.87	0.67	0.89
	S.E.	0.16	0.27	0.21	0.20
	N	20	10	10	20
1 TO 2	MEAN	0.5	0.4	0.3	0.6
	S.D.	0.62	0.42	0.78	0.78
	S.E.	0.14	0.13	0.25	0.17
	N	20	10	10	20
2 TO 3	MEAN	-0.1	0.1	-0.1	0.3
	S.D.	0.72	0.63	0.53	0.54
	S.E.	0.16	0.20	0.17	0.12
	N	20	10	10	20

** = Significantly different from the control group at 0.01 using Dunnett's test

PROJECT NO.: WIL-189207M
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SPONSOR NO.: DUPONT-24459

TABLE 15 (DOSING PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHT CHANGES [G]

PAGE 2

WEEK	3 TO	4	MALES		
			0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY
	MEAN		1.5	1.1	1.4
	S.D.		0.64	0.58	0.69
	S.E.		0.14	0.18	0.22
	N		20	10	10
					20

None significantly different from control group

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
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SPONSOR NO.: DUPONT-24459

TABLE 16 (DOSING PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHT CHANGES [G]

PAGE 1

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
WEEK -2 TO -1				
MEAN	1.5	2.0	2.0	1.8
S.D.	1.04	1.17	0.73	0.72
S.E.	0.23	0.37	0.23	0.16
N	20	10	10	20
-1 TO 0				
MEAN	0.8	0.3	0.1*	0.1**
S.D.	0.61	0.67	0.52	0.64
S.E.	0.14	0.21	0.16	0.14
N	20	10	10	20
0 TO 1				
MEAN	0.1	0.4	0.5	0.7
S.D.	0.67	0.79	0.69	0.75
S.E.	0.15	0.25	0.22	0.17
N	20	10	10	20
1 TO 2				
MEAN	0.5	0.9	0.4	1.1
S.D.	1.15	0.89	0.57	0.75
S.E.	0.26	0.28	0.18	0.17
N	20	10	10	19
2 TO 3				
MEAN	0.2	0.7	0.8	0.9
S.D.	1.68	1.06	0.81	0.77
S.E.	0.38	0.34	0.26	0.18
N	20	10	10	19

* = Significantly different from the control group at 0.05 using Dunnett's test

** = Significantly different from the control group at 0.01 using Dunnett's test

PROJECT NO.: WIL-189207F
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TABLE 16 (DOSING PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHT CHANGES [G]

PAGE 2

WEEK	3 TO 4	FEMALES		
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY
	MEAN	0.6	0.6	1.0
	S.D.	0.76	0.86	0.59
	S.E.	0.17	0.27	0.19
	N	19	10	10
				19

None significantly different from control group

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04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 17 (RECOVERY PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHT CHANGES [G]

PAGE 1

WEEK	4 TO 5	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	
MEAN		0.9			-0.4**
S.D.		0.82			0.85
S.E.		0.26			0.27
N		10			10
5 TO 6					
MEAN		1.5			0.8*
S.D.		0.64			0.70
S.E.		0.20			0.22
N		10			10
6 TO 7					
MEAN		0.2			-0.4*
S.D.		0.65			0.53
S.E.		0.20			0.17
N		10			10
7 TO 8					
MEAN		0.9			0.6
S.D.		0.67			0.32
S.E.		0.21			0.10
N		10			10
8 TO 9					
MEAN		0.6			0.3
S.D.		0.44			0.49
S.E.		0.14			0.15
N		10			10

* = Significantly different from the control group at 0.05 using Dunnett's test

** = Significantly different from the control group at 0.01 using Dunnett's test

NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 18 (RECOVERY PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF BODY WEIGHT CHANGES [G]

PAGE 1

WEEK	4 TO 5	FEMALES			PAGE 1
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	
	MEAN	0.5	NA	NA	-0.4*
	S.D.	0.48			1.06
	S.E.	0.16			0.35
	N	9			9
	5 TO 6	0.0	NA	NA	0.1
	MEAN				0.49
	S.D.	1.11			0.16
	S.E.	0.37			9
	N	9			
	6 TO 7	0.4	NA	NA	0.0
	MEAN				0.64
	S.D.	1.07			0.21
	S.E.	0.36			9
	N	9			
	7 TO 8	0.1	NA	NA	0.3
	MEAN				0.85
	S.D.	1.12			0.28
	S.E.	0.37			9
	N	9			
	8 TO 9	0.6	NA	NA	0.9
	MEAN				0.71
	S.D.	0.72			0.24
	S.E.	0.24			9
	N	9			

* = Significantly different from the control group at 0.05 using Dunnett's test

NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 19 (DOSING PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF CUMULATIVE BODY WEIGHT CHANGES [G]

PAGE 1

		MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
WEEK	0 TO 1				
	MEAN	1.1	1.3	1.7	2.5**
	S.D.	0.74	0.87	0.67	0.89
	S.E.	0.16	0.27	0.21	0.20
	N	20	10	10	20
0 TO 2					
	MEAN	1.7	1.6	2.1	3.1**
	S.D.	1.11	1.09	1.04	1.37
	S.E.	0.25	0.34	0.33	0.31
	N	20	10	10	20
0 TO 3					
	MEAN	1.6	1.7	2.0	3.4**
	S.D.	1.37	1.44	1.19	1.66
	S.E.	0.31	0.46	0.38	0.37
	N	20	10	10	20
0 TO 4					
	MEAN	3.2	2.9	3.4	5.4**
	S.D.	1.47	1.64	1.32	1.83
	S.E.	0.33	0.52	0.42	0.41
	N	20	10	10	20

** = Significantly different from the control group at 0.01 using Dunnett's test

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 20 (DOSING PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF CUMULATIVE BODY WEIGHT CHANGES [G]

PAGE 1

WEEK	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
0 TO 1	MEAN	0.1	0.4	0.5	0.7
	S.D.	0.67	0.79	0.69	0.75
	S.E.	0.15	0.25	0.22	0.17
	N	20	10	10	20
0 TO 2	MEAN	0.6	1.3	0.9	1.8**
	S.D.	1.10	1.02	0.70	1.08
	S.E.	0.25	0.32	0.22	0.25
	N	20	10	10	19
0 TO 3	MEAN	0.8	2.0	1.6	2.7**
	S.D.	1.99	1.23	1.04	1.34
	S.E.	0.44	0.39	0.33	0.31
	N	20	10	10	19
0 TO 4	MEAN	1.7	2.6	2.6	3.6**
	S.D.	1.51	0.74	0.85	1.45
	S.E.	0.35	0.23	0.27	0.33
	N	19	10	10	19

** = Significantly different from the control group at 0.01 using Dunnett's test

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

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PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 21 (RECOVERY PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF CUMULATIVE BODY WEIGHT CHANGES [G]

PAGE 1

WEEK	4 TO	5	MALES		
			0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY
		MEAN	0.9	NA	NA
		S.D.	0.82		-0.4**
		S.E.	0.26		0.85
		N	10		0.27
					10
	4 TO	6	2.4	NA	NA
		MEAN	0.96		0.3**
		S.D.	0.96		0.96
		S.E.	0.30		0.30
		N	10		10
	4 TO	7	2.7	NA	NA
		MEAN	1.10		-0.1**
		S.D.	0.35		1.13
		S.E.			0.36
		N	10		10
	4 TO	8	3.6	NA	NA
		MEAN	1.38		0.5**
		S.D.	0.44		0.99
		S.E.			0.31
		N	10		10
	4 TO	9	4.2	NA	NA
		MEAN	1.53		0.8**
		S.D.	0.48		1.04
		S.E.			0.33
		N	10		10

** = Significantly different from the control group at 0.01 using Dunnett's test
NA = NOT APPLICABLE

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04/21/2008

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 22 (RECOVERY PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF CUMULATIVE BODY WEIGHT CHANGES [G]

PAGE 1

WEEK	4 TO	5	FEMALES			
			0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
		MEAN	0.5	NA	NA	-0.4*
		S.D.	0.48			1.06
		S.E.	0.16			0.35
		N	9			9
	4 TO	6	0.4	NA	NA	-0.3
		S.D.	1.08			1.08
		S.E.	0.36			0.36
		N	9			9
	4 TO	7	0.8	NA	NA	-0.4*
		S.D.	1.10			1.01
		S.E.	0.37			0.34
		N	9			9
	4 TO	8	0.9	NA	NA	0.0
79		S.D.	0.61			1.27
		S.E.	0.20			0.42
		N	9			9
	4 TO	9	1.6	NA	NA	0.8
		S.D.	1.04			1.90
		S.E.	0.35			0.63
		N	9			9

* = Significantly different from the control group at 0.05 using Dunnett's test

NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 23 (DOSING PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF FOOD CONSUMPTION [G/ANIMAL/DAY]

PAGE 1

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
WEEK -2 TO -1				
MEAN	5.9	6.2	5.7	6.5
S.D.	0.76	0.73	0.79	1.43
S.E.	0.17	0.23	0.25	0.32
N	20	10	10	20
0 TO 1				
MEAN	5.5	5.3	5.6	5.7
S.D.	0.69	0.37	1.32	0.84
S.E.	0.16	0.12	0.44	0.19
N	19	10	9	20
1 TO 2				
MEAN	5.7	5.8	5.4	6.1
S.D.	1.12	1.28	0.87	1.25
S.E.	0.25	0.41	0.28	0.29
N	20	10	10	18
2 TO 3				
MEAN	5.8	5.7	5.8	6.8
S.D.	1.03	1.53	1.16	1.51
S.E.	0.24	0.48	0.37	0.37
N	19	10	10	17
3 TO 4				
MEAN	5.6	5.7	5.8	6.4
S.D.	0.94	1.19	1.37	1.28
S.E.	0.22	0.38	0.43	0.30
N	19	10	10	18

None significantly different from control group

PBFSTv5.28
04/22/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 24 (DOSING PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF FOOD CONSUMPTION [G/ANIMAL/DAY]

PAGE 1

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
WEEK -2 TO -1				
MEAN	5.3	5.6	5.7	5.5
S.D.	0.85	1.09	1.40	1.13
S.E.	0.20	0.34	0.44	0.26
N	18	10	10	19
0 TO 1				
MEAN	5.3	6.1	6.1	5.4
S.D.	1.05	1.78	2.06	1.50
S.E.	0.25	0.59	0.69	0.34
N	18	9	9	19
1 TO 2				
MEAN	5.3	5.8	6.1	5.6
S.D.	1.46	1.40	1.82	1.54
S.E.	0.33	0.47	0.58	0.35
N	20	9	10	19
2 TO 3				
MEAN	5.6	5.6	5.4	5.8
S.D.	1.67	1.38	0.90	1.39
S.E.	0.39	0.49	0.30	0.34
N	18	8	9	17
3 TO 4				
MEAN	5.9	6.3	5.9	6.1
S.D.	1.29	1.91	1.35	1.28
S.E.	0.30	0.60	0.43	0.29
N	18	10	10	19

None significantly different from control group

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 25 (RECOVERY PERIOD - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF FOOD CONSUMPTION [G/ANIMAL/DAY]

PAGE 1

WEEK	4 TO 5	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
	MEAN	5.5	NA	NA	6.0
	S.D.	0.62			0.87
	S.E.	0.20			0.28
	N	10			10
	5 TO 6	5.6	NA	NA	5.4
	S.D.	0.67			0.62
	S.E.	0.21			0.19
	N	10			10
	6 TO 7	5.3	NA	NA	5.0
	S.D.	0.63			0.48
	S.E.	0.20			0.15
	N	10			10
	7 TO 8	5.4	NA	NA	5.1
	S.D.	0.76			0.73
	S.E.	0.24			0.23
	N	10			10
	8 TO 9	5.5	NA	NA	4.9*
	S.D.	0.53			0.56
	S.E.	0.17			0.18
	N	10			10

* = Significantly different from the control group at 0.05 using Dunnett's test

NA = NOT APPLICABLE

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04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 26 (RECOVERY PERIOD - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF FOOD CONSUMPTION [G/ANIMAL/DAY]

PAGE 1

WEEK	4 TO 5	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	
	MEAN	6.1	NA	NA	5.5
	S.D.	1.72			0.91
	S.E.	0.57			0.32
	N	9			8
	5 TO 6	6.1	NA	NA	5.8
	MEAN	1.98			1.71
	S.D.	0.70			0.60
	N	8			8
	6 TO 7	5.4	NA	NA	4.7
	MEAN	2.10			0.44
	S.D.	0.70			0.17
	N	9			7
	7 TO 8	5.5	NA	NA	5.8
	MEAN	2.01			1.95
	S.D.	0.71			0.69
	N	8			8
	8 TO 9	4.8	NA	NA	5.1
	MEAN	0.90			1.54
	S.D.	0.34			0.55
	N	7			8

None significantly different from control group

NA = NOT APPLICABLE

PBFSTv5.28
04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 1

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
WHITE CELLS (thous/uL)					
WEEK 4	MEAN	4.16	3.18	5.26	5.34
% DIFFERENCE			-23.6	26.4	28.4
S.D.		1.078	0.921	2.553	2.049
S.E.		0.359	0.326	0.903	0.683
N		9	8	8	9
WEEK 8	MEAN	5.25	NA	NA	6.79*
% DIFFERENCE					29.3
S.D.		1.042			1.798
S.E.		0.330			0.568
N		10			10
RED CELLS (mil/uL)					
WEEK 4	MEAN	8.80	8.44	8.28	8.13*
% DIFFERENCE			-4.1	-5.9	-7.6
S.D.		0.519	0.421	0.401	0.447
S.E.		0.173	0.149	0.142	0.149
N		9	8	8	9
WEEK 8	MEAN	9.21	NA	NA	9.38
% DIFFERENCE					1.8
S.D.		0.346			0.538
S.E.		0.110			0.170
N		10			10

thous/uL = THOUSANDS/MICROLITER, mil/uL = MILLIONS/MICROLITER, fL = FEMTOLITERS, pg = PICOGRAMS, g/dL = GRAMS/DECILITER

* = Significantly different from the control group at 0.05 using Dunnett's test

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 2

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
HEMOGLOBIN (g/dL)					
WEEK 4	MEAN	14.1	13.8	13.4*	13.1**
% DIFFERENCE			-2.1	-5.0	-7.1
S.D.		0.53	0.45	0.46	0.53
S.E.		0.18	0.16	0.16	0.18
N		9	8	8	9
WEEK 8	MEAN	15.0	NA	NA	14.7
% DIFFERENCE					-2.0
S.D.		0.43			0.75
S.E.		0.14			0.24
N		10			10
HEMATOCRIT (%)					
WEEK 4	MEAN	40.1	38.8	38.1*	37.5**
% DIFFERENCE			-3.2	-5.0	-6.5
S.D.		1.72	1.06	1.36	1.54
S.E.		0.57	0.38	0.48	0.51
N		9	8	8	9
WEEK 8	MEAN	43.4	NA	NA	41.9
% DIFFERENCE					-3.5
S.D.		1.20			2.05
S.E.		0.38			0.65
N		10			10

thous/uL = THOUSANDS/MICROLITER, mil/uL = MILLIONS/MICROLITER, fL = FEMTOLITERS, pg = PICOGRAMS, g/dL = GRAMS/DECILITER

* = Significantly different from the control group at 0.05 using Dunnett's test

** = Significantly different from the control group at 0.01 using Dunnett's test

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 3

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
MCV (fL)					
WEEK 4	MEAN	45.6	46.1	46.0	46.3
% DIFFERENCE			1.1	0.9	1.5
S.D.		1.40	1.12	1.15	1.42
S.E.		0.47	0.40	0.41	0.47
N		9	8	8	9
WEEK 8	MEAN	47.2	NA	NA	44.7**
% DIFFERENCE					-5.3
S.D.		1.58			1.19
S.E.		0.50			0.38
N		10			10
MCH (pg)					
WEEK 4	MEAN	16.0	16.4	16.2	16.1
% DIFFERENCE			2.5	1.3	0.6
S.D.		0.59	0.37	0.45	0.58
S.E.		0.20	0.13	0.16	0.19
N		9	8	8	9
WEEK 8	MEAN	16.3	NA	NA	15.7**
% DIFFERENCE					-3.7
S.D.		0.59			0.29
S.E.		0.19			0.09
N		10			10

thous/uL = THOUSANDS/MICROLITER, mil/uL = MILLIONS/MICROLITER, fL = FEMTOLITERS, pg = PICOGRAMS, g/dL = GRAMS/DECILITER

** = Significantly different from the control group at 0.01 using Dunnett's test
NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 4

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
MCHC (g/dL)					
WEEK 4	MEAN	35.2	35.6	35.2	34.9
% DIFFERENCE			1.1	0.0	-0.9
S.D.		0.81	0.53	0.47	0.55
S.E.		0.27	0.19	0.17	0.18
N		9	8	8	9
WEEK 8	MEAN	34.6	NA	NA	35.1
% DIFFERENCE					1.4
S.D.		0.62			0.36
S.E.		0.20			0.11
N		10			10
PLATELET (thous/uL)					
WEEK 4	MEAN	1163.	1284.	1230.	1147.
% DIFFERENCE			10.4	5.8	-1.4
S.D.		76.7	185.7	150.4	99.9
S.E.		25.6	65.7	53.2	33.3
N		9	8	8	9
WEEK 8	MEAN	1290.	NA	NA	1452.*
% DIFFERENCE					12.6
S.D.		185.9			143.0
S.E.		58.8			45.2
N		10			10

thous/uL = THOUSANDS/MICROLITER, mil/uL = MILLIONS/MICROLITER, fL = FEMTOLITERS, pg = PICOGRAMS, g/dL = GRAMS/DECILITER

* = Significantly different from the control group at 0.05 using Dunnett's test

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 5

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
RETICULOCYTE (%)					
WEEK 4	MEAN	3.4	3.3	3.5	3.8
% DIFFERENCE			-2.9	2.9	11.8
S.D.		0.48	0.35	0.27	0.55
S.E.		0.16	0.13	0.09	0.18
N		9	8	8	9
WEEK 8	MEAN	2.9	NA	NA	2.9
% DIFFERENCE					0.0
S.D.		0.41			0.43
S.E.		0.13			0.14
N		10			10
RETIC ABSOLUTE (thous/uL)					
WEEK 4	MEAN	298.0	278.6	285.2	307.4
% DIFFERENCE			-6.5	-4.3	3.2
S.D.		57.23	30.59	21.41	29.76
S.E.		19.08	10.82	7.57	9.92
N		9	8	8	9
WEEK 8	MEAN	263.7	NA	NA	266.5
% DIFFERENCE					1.1
S.D.		36.14			39.10
S.E.		11.43			12.36
N		10			10

thous/uL = THOUSANDS/MICROLITER, mil/uL = MILLIONS/MICROLITER, fL = FEMTOLITERS, pg = PICOGRAMS, g/dL = GRAMS/DECILITER

None significantly different from control group

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TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 6

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
NEUTROPHIL (%)					
WEEK 4	MEAN	22.9	20.5	21.1	25.5
% DIFFERENCE			-10.5	-7.9	11.4
S.D.		4.03	4.79	4.71	5.63
S.E.		1.34	1.69	1.66	1.88
N		9	8	8	9
WEEK 8	MEAN	21.6	NA	NA	18.7
% DIFFERENCE					-13.4
S.D.		8.80			7.25
S.E.		2.78			2.29
N		10			10
LYMPHOCYTE (%)					
WEEK 4	MEAN	70.8	73.8	72.4	66.2
% DIFFERENCE			4.2	2.3	-6.5
S.D.		4.95	4.89	6.12	5.47
S.E.		1.65	1.73	2.16	1.82
N		9	8	8	9
WEEK 8	MEAN	71.8	NA	NA	75.3
% DIFFERENCE					4.9
S.D.		8.78			8.44
S.E.		2.78			2.67
N		10			10

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None significantly different from control group

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TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 7

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
MONOCYTE (%)					
WEEK 4	MEAN	2.4	2.2	2.6	4.7**
% DIFFERENCE			-8.3	8.3	95.8
S.D.		1.12	0.96	1.20	1.63
S.E.		0.37	0.34	0.42	0.54
N		9	8	8	9
WEEK 8	MEAN	2.3	NA	NA	2.0
% DIFFERENCE					-13.0
S.D.		1.03			0.91
S.E.		0.33			0.29
N		10			10
EOSINOPHIL (%)					
WEEK 4	MEAN	3.3	3.1	3.1	2.1
% DIFFERENCE			-6.1	-6.1	-36.4
S.D.		1.03	1.08	1.35	1.04
S.E.		0.34	0.38	0.48	0.35
N		9	8	8	9
WEEK 8	MEAN	3.7	NA	NA	3.3
% DIFFERENCE					-10.8
S.D.		3.70			3.57
S.E.		1.17			1.13
N		10			10

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TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 8

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
BASOPHIL (%)					
WEEK 4	MEAN	0.1	0.2	0.2	0.2
% DIFFERENCE			100.0	100.0	100.0
S.D.		0.09	0.15	0.09	0.24
S.E.		0.03	0.05	0.03	0.08
N		9	8	8	9
WEEK 8	MEAN	0.2	NA	NA	0.2
% DIFFERENCE					0.0
S.D.		0.16			0.19
S.E.		0.05			0.06
N		10			10
LG UNSTAIN CELL (%)					
WEEK 4	MEAN	0.5	0.4	0.6	1.3**
% DIFFERENCE			-20.0	20.0	160.0
S.D.		0.27	0.22	0.30	0.59
S.E.		0.09	0.08	0.10	0.20
N		9	8	8	9
WEEK 8	MEAN	0.4	NA	NA	0.4
% DIFFERENCE					0.0
S.D.		0.23			0.28
S.E.		0.07			0.09
N		10			10

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TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 9

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
NEU ABSOLUTE (thous/uL)					
WEEK 4	MEAN	0.94	0.66	1.09	1.28
% DIFFERENCE			-29.8	16.0	36.2
S.D.		0.235	0.293	0.565	0.371
S.E.		0.078	0.104	0.200	0.124
N		9	8	8	9
WEEK 8	MEAN	1.09	NA	NA	1.27
% DIFFERENCE					16.5
S.D.		0.392			0.639
S.E.		0.124			0.202
N		10			10
LYMPH ABSOLUTE (thous/uL)					
WEEK 4	MEAN	2.96	2.35	3.84	3.62
% DIFFERENCE			-20.6	29.7	22.3
S.D.		0.830	0.664	1.913	1.513
S.E.		0.277	0.235	0.676	0.504
N		9	8	8	9
WEEK 8	MEAN	3.80	NA	NA	5.13*
% DIFFERENCE					35.0
S.D.		0.996			1.543
S.E.		0.315			0.488
N		10			10

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PROJECT NO.: WIL-189207M
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SPONSOR NO.: DUPONT-24459

TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 10

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
MONO ABSOLUTE (thous/uL)					
WEEK 4	MEAN	0.10	0.07	0.12	0.27**
% DIFFERENCE			-30.0	20.0	170.0
S.D.		0.048	0.029	0.062	0.146
S.E.		0.016	0.010	0.022	0.049
N		9	8	8	9
WEEK 8	MEAN	0.12	NA	NA	0.14
% DIFFERENCE					16.7
S.D.		0.049			0.071
S.E.		0.015			0.023
N		10			10
EOS ABSOLUTE (thous/uL)					
WEEK 4	MEAN	0.14	0.10	0.16	0.10
% DIFFERENCE			-28.6	14.3	-28.6
S.D.		0.069	0.045	0.113	0.050
S.E.		0.023	0.016	0.040	0.017
N		9	8	8	9
WEEK 8	MEAN	0.20	NA	NA	0.21
% DIFFERENCE					5.0
S.D.		0.222			0.227
S.E.		0.070			0.072
N		10			10

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TABLE 27 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

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ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
BASO ABSOLUTE (thous/uL)					
WEEK 4	MEAN	0.01	0.00	0.01	0.01
% DIFFERENCE			-100.0	0.0	0.0
S.D.		0.005	0.005	0.005	0.008
S.E.		0.002	0.002	0.002	0.003
N		9	8	8	9
WEEK 8	MEAN	0.01	NA	NA	0.01
% DIFFERENCE					0.0
S.D.		0.009			0.015
S.E.		0.003			0.005
N		10			10
LUC ABSOLUTE (thous/uL)					
WEEK 4	MEAN	0.02	0.01	0.04	0.07**
% DIFFERENCE			-50.0	100.0	250.0
S.D.		0.013	0.008	0.031	0.055
S.E.		0.004	0.003	0.011	0.018
N		9	8	8	9
WEEK 8	MEAN	0.02	NA	NA	0.03
% DIFFERENCE					50.0
S.D.		0.015			0.020
S.E.		0.005			0.006
N		10			10

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PCPSv5.24
04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 1

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
WHITE CELLS (thous/uL)					
WEEK 4	MEAN	2.40	4.91	4.81	4.66
% DIFFERENCE			104.6	100.4	94.2
S.D.		0.559	1.742	1.178	1.917
S.E.		0.395	0.711	0.680	0.857
N		2	6	3	5
WEEK 8	MEAN	5.15	NA	NA	5.38
% DIFFERENCE					4.5
S.D.		2.021			2.185
S.E.		0.715			0.728
N		8			9
RED CELLS (mil/uL)					
WEEK 4	MEAN	8.71	9.13	8.64	8.65
% DIFFERENCE			4.8	-0.8	-0.7
S.D.		0.028	0.308	0.575	0.403
S.E.		0.020	0.126	0.332	0.180
N		2	6	3	5
WEEK 8	MEAN	9.10	NA	NA	9.45
% DIFFERENCE					3.8
S.D.		0.707			0.399
S.E.		0.250			0.133
N		8			9

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None significantly different from control group

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PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 2

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>					
HEMOGLOBIN (g/dL)					
WEEK 4	MEAN	13.7	14.5	13.8	13.9
	% DIFFERENCE		5.8	0.7	1.5
	S.D.	0.64	0.46	0.89	0.26
	S.E.	0.45	0.19	0.51	0.12
	N	2	6	3	5
WEEK 8	MEAN	14.4	NA	NA	14.9
	% DIFFERENCE				3.5
	S.D.	1.25			0.99
	S.E.	0.44			0.33
	N	8			9
<hr/>					
HEMATOCRIT (%)					
WEEK 4	MEAN	41.9	41.8	39.9	40.3
	% DIFFERENCE		-0.2	-4.8	-3.8
	S.D.	1.56	1.87	2.58	1.25
	S.E.	1.10	0.76	1.49	0.56
	N	2	6	3	5
WEEK 8	MEAN	41.0	NA	NA	42.7
	% DIFFERENCE				4.1
	S.D.	3.11			2.81
	S.E.	1.10			0.94
	N	8			9

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TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 3

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
MCV (fL)					
WEEK 4	MEAN	48.1	45.8	46.1	46.6
% DIFFERENCE			-4.8	-4.2	-3.1
S.D.		1.70	1.84	0.76	1.65
S.E.		1.20	0.75	0.44	0.74
N		2	6	3	5
WEEK 8	MEAN	45.1	NA	NA	45.1
% DIFFERENCE					0.0
S.D.		2.53			2.21
S.E.		0.90			0.74
N		8			9
MCH (pg)					
WEEK 4	MEAN	15.7	15.9	16.0	16.1
% DIFFERENCE			1.3	1.9	2.5
S.D.		0.71	0.51	0.36	0.74
S.E.		0.50	0.21	0.21	0.33
N		2	6	3	5
WEEK 8	MEAN	15.9	NA	NA	15.7
% DIFFERENCE					-1.3
S.D.		0.98			0.70
S.E.		0.35			0.23
N		8			9

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None significantly different from control group

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PROJECT NO.: WIL-189207F
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SPONSOR NO.: DUPONT-24459

TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 4

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
MCHC (g/dL)					
WEEK 4	MEAN	32.7	34.8	34.7	34.5
	% DIFFERENCE		6.4	6.1	5.5
	S.D.	0.28	0.48	0.15	0.63
	S.E.	0.20	0.20	0.09	0.28
	N	2	6	3	5
WEEK 8	MEAN	35.1	NA	NA	34.9
	% DIFFERENCE				-0.6
	S.D.	0.58			0.64
	S.E.	0.20			0.21
	N	8			9
PLATELET (thous/uL)					
WEEK 4	MEAN	785.	935.	763.	986.
	% DIFFERENCE		19.1	-2.8	25.6
	S.D.	153.4	187.9	561.5	304.7
	S.E.	108.5	76.7	324.2	136.3
	N	2	6	3	5
WEEK 8	MEAN	1235.	NA	NA	1105.
	% DIFFERENCE				-10.5
	S.D.	168.8			224.4
	S.E.	59.7			74.8
	N	8			9

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TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 5

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
RETICULOCYTE (%)					
WEEK 4	MEAN	3.5	3.0	3.2	3.1
% DIFFERENCE			-14.3	-8.6	-11.4
S.D.		0.28	0.39	0.30	0.48
S.E.		0.20	0.16	0.17	0.21
N		2	6	3	5
WEEK 8	MEAN	2.8	NA	NA	2.8
% DIFFERENCE					0.0
S.D.		0.39			0.60
S.E.		0.14			0.20
N		8			9
RETIC ABSOLUTE (thous/uL)					
WEEK 4	MEAN	303.3	276.1	273.9	264.5
% DIFFERENCE			-9.0	-9.7	-12.8
S.D.		23.97	36.20	8.55	33.70
S.E.		16.95	14.78	4.94	15.07
N		2	6	3	5
WEEK 8	MEAN	253.8	NA	NA	269.6
% DIFFERENCE					6.2
S.D.		27.68			61.54
S.E.		9.79			20.51
N		8			9

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PROJECT NO.: WIL-189207F
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TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 6

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
NEUTROPHIL (%)					
WEEK 4	MEAN	16.3	18.1	18.7	18.0
% DIFFERENCE			11.0	14.7	10.4
S.D.		2.47	5.87	9.01	5.12
S.E.		1.75	2.40	5.20	2.29
N		2	6	3	5
WEEK 8	MEAN	19.4	NA	NA	17.5
% DIFFERENCE					-9.8
S.D.		11.83			13.57
S.E.		4.18			4.52
N		8			9
LYMPHOCYTE (%)					
WEEK 4	MEAN	74.6	74.9	73.8	75.0
% DIFFERENCE			0.4	-1.1	0.5
S.D.		4.81	8.23	9.32	6.46
S.E.		3.40	3.36	5.38	2.89
N		2	6	3	5
WEEK 8	MEAN	75.3	NA	NA	76.9
% DIFFERENCE					2.1
S.D.		13.52			13.67
S.E.		4.78			4.56
N		8			9

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TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 7

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
MONOCYTE (%)					
WEEK 4	MEAN	3.1	2.2	2.8	3.0
% DIFFERENCE			-29.0	-9.7	-3.2
S.D.		0.14	0.83	0.90	0.95
S.E.		0.10	0.34	0.52	0.43
N		2	6	3	5
WEEK 8	MEAN	2.9	NA	NA	2.2
% DIFFERENCE					-24.1
S.D.		1.54			0.69
S.E.		0.54			0.23
N		8			9
EOSINOPHIL (%)					
WEEK 4	MEAN	5.6	3.9	4.1	3.0
% DIFFERENCE			-30.4	-26.8	-46.4
S.D.		6.51	2.29	0.78	1.16
S.E.		4.60	0.93	0.45	0.52
N		2	6	3	5
WEEK 8	MEAN	1.6	NA	NA	2.6
% DIFFERENCE					62.5
S.D.		1.07			1.57
S.E.		0.38			0.52
N		8			9

thous/uL = THOUSANDS/MICROLITER, mil/uL = MILLIONS/MICROLITER, fL = FEMTOLITERS, pg = PICOGRAMS, g/dL = GRAMS/DECILITER

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 8

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>					
BASOPHIL (%)					
WEEK 4	MEAN	0.2	0.3	0.2	0.3
	% DIFFERENCE		50.0	0.0	50.0
	S.D.	0.28	0.12	0.06	0.15
	S.E.	0.20	0.05	0.03	0.07
	N	2	6	3	5
WEEK 8	MEAN	0.1	NA	NA	0.1
	% DIFFERENCE				0.0
	S.D.	0.14			0.10
	S.E.	0.05			0.03
	N	8			9
<hr/>					
LG UNSTAIN CELL (%)					
WEEK 4	MEAN	0.2	0.6	0.4	0.8
	% DIFFERENCE		200.0	100.0	300.0
	S.D.	0.21	0.12	0.21	0.41
	S.E.	0.15	0.05	0.12	0.19
	N	2	6	3	5
WEEK 8	MEAN	0.8	NA	NA	0.7
	% DIFFERENCE				-12.5
	S.D.	1.20			0.73
	S.E.	0.42			0.24
	N	8			9

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None significantly different from control group

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PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 9

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
NEU ABSOLUTE (thous/uL)					
WEEK 4	MEAN	0.39	0.87	0.87	0.77
% DIFFERENCE			123.1	123.1	97.4
S.D.		0.035	0.329	0.340	0.123
S.E.		0.025	0.134	0.197	0.055
N		2	6	3	5
WEEK 8	MEAN	1.15	NA	NA	1.02
% DIFFERENCE					-11.3
S.D.		1.308			1.148
S.E.		0.462			0.383
N		8			9
LYMPH ABSOLUTE (thous/uL)					
WEEK 4	MEAN	1.78	3.72	3.58	3.58
% DIFFERENCE			109.0	101.1	101.1
S.D.		0.304	1.520	1.115	1.727
S.E.		0.215	0.621	0.644	0.772
N		2	6	3	5
WEEK 8	MEAN	3.70	NA	NA	4.04
% DIFFERENCE					9.2
S.D.		0.983			1.724
S.E.		0.348			0.575
N		8			9

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None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

PAGE 10

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
MONO ABSOLUTE (thous/uL)					
WEEK 4	MEAN	0.08	0.10	0.13	0.13
% DIFFERENCE			25.0	62.5	62.5
S.D.		0.021	0.031	0.026	0.058
S.E.		0.015	0.013	0.015	0.026
N		2	6	3	5
WEEK 8	MEAN	0.16	NA	NA	0.11
% DIFFERENCE					-31.3
S.D.		0.123			0.037
S.E.		0.043			0.012
N		8			9
EOS ABSOLUTE (thous/uL)					
WEEK 4	MEAN	0.16	0.18	0.20	0.13
% DIFFERENCE			12.5	25.0	-18.8
S.D.		0.191	0.092	0.083	0.048
S.E.		0.135	0.037	0.048	0.021
N		2	6	3	5
WEEK 8	MEAN	0.08	NA	NA	0.14
% DIFFERENCE					75.0
S.D.		0.053			0.105
S.E.		0.019			0.035
N		8			9

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None significantly different from control group

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PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 28 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF HEMATOLOGY VALUES

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ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
BASO ABSOLUTE (thous/uL)					
WEEK 4	MEAN	0.01	0.01	0.01	0.01
% DIFFERENCE			0.0	0.0	0.0
S.D.		0.007	0.010	0.000	0.004
S.E.		0.005	0.004	0.000	0.002
N		2	6	3	5
WEEK 8	MEAN	0.01	NA	NA	0.01
% DIFFERENCE					0.0
S.D.		0.010			0.006
S.E.		0.004			0.002
N		8			9
LUC ABSOLUTE (thous/uL)					
WEEK 4	MEAN	0.01	0.03	0.02	0.04
% DIFFERENCE			200.0	100.0	300.0
S.D.		0.007	0.016	0.015	0.040
S.E.		0.005	0.007	0.009	0.018
N		2	6	3	5
WEEK 8	MEAN	0.06	NA	NA	0.05
% DIFFERENCE					-16.7
S.D.		0.112			0.058
S.E.		0.040			0.019
N		8			9

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None significantly different from control group

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 29 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 1

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
AERBUMIN (g/dL)					
WEEK 4	MEAN	3.2	3.2	3.3	4.2**
% DIFFERENCE		0.0	3.1	31.3	
S.D.		0.17	0.22	0.18	0.36
S.E.		0.05	0.07	0.06	0.11
N		10	10	10	10
WEEK 8	MEAN	3.2	NA	NA	3.2
% DIFFERENCE		0.0			0.0
S.D.		0.17			0.21
S.E.		0.05			0.07
N		10			10
TOTAL PROTEIN (g/dL)					
WEEK 4	MEAN	5.3	5.2	5.0	6.0**
% DIFFERENCE		-1.9	-5.7	13.2	
S.D.		0.24	0.35	0.22	0.51
S.E.		0.08	0.11	0.07	0.16
N		10	10	10	10
WEEK 8	MEAN	5.5	NA	NA	5.5
% DIFFERENCE		0.0			0.0
S.D.		0.60			0.33
S.E.		0.19			0.10
N		10			10

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** = Significantly different from the control group at 0.01 using Dunnett's test

NA = NOT APPLICABLE

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TABLE 29 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
GLOBULIN (g/dL)					
WEEK 4	MEAN	2.1	2.1	1.7**	1.8**
% DIFFERENCE		0.0	-19.0	-14.3	
S.D.		0.14	0.18	0.16	0.22
S.E.		0.04	0.06	0.05	0.07
N		10	10	10	10
WEEK 8	MEAN	2.3	NA	NA	2.4
% DIFFERENCE		0.53			4.3
S.D.		0.17			0.30
S.E.		10			0.10
					10
A/G RATIO					
WEEK 4	MEAN	1.54	1.56	1.92**	2.32**
% DIFFERENCE		1.3	24.7	50.6	
S.D.		0.134	0.128	0.222	0.241
S.E.		0.042	0.040	0.070	0.076
N		10	10	10	10
WEEK 8	MEAN	1.43	NA	NA	1.34
% DIFFERENCE		0.246			-6.3
S.D.		0.078			0.214
S.E.		10			0.068
					10

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PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 29 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 3

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>					
TOTAL BILI (mg/dL)					
WEEK 4	MEAN	0.1	0.1	0.1	0.2
% DIFFERENCE			0.0	0.0	100.0
S.D.		0.07	0.05	0.07	0.08
S.E.		0.02	0.02	0.02	0.02
N		10	10	10	10
WEEK 8	MEAN	0.1	NA	NA	0.1
% DIFFERENCE					0.0
S.D.		0.00			0.04
S.E.		0.00			0.01
N		10			10
<hr/>					
UREA NITROGEN (mg/dL)					
WEEK 4	MEAN	20.1	19.3	22.3	24.5*
% DIFFERENCE			-4.0	10.9	21.9
S.D.		1.84	2.82	4.89	3.49
S.E.		0.61	0.89	1.55	1.10
N		9	10	10	10
WEEK 8	MEAN	24.4	NA	NA	21.6
% DIFFERENCE					-11.5
S.D.		7.18			3.60
S.E.		2.71			1.20
N		7			9

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* = Significantly different from the control group at 0.05 using Dunnett's test

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 29 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 4

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
CREATININE (mg/dL)					
WEEK 4	MEAN	2.6	0.1	2.6	0.0
% DIFFERENCE			-96.2	0.0	-100.0
S.D.		0.71	0.08	0.00	0.00
S.E.		0.50	0.04	0.00	0.00
N		2	4	1	5
WEEK 8	MEAN	0.2	NA	NA	0.0
% DIFFERENCE					-100.0
S.D.		0.34			0.05
S.E.		0.17			0.02
N		4			7
ALKALINEPHOS/TSE (U/L)					
WEEK 4	MEAN	88.	73.	144.	1163.**
% DIFFERENCE			-17.0	63.6	1221.6
S.D.		29.5	18.2	51.2	682.4
S.E.		9.3	5.8	16.2	215.8
N		10	10	10	10
WEEK 8	MEAN	55.	NA	NA	63.
% DIFFERENCE					14.5
S.D.		9.2			19.4
S.E.		2.9			6.1
N		10			10

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NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 29 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 5

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
ALANINE TRANSFER (U/L)					
WEEK 4	MEAN	52.	38.	82.	704.**
% DIFFERENCE			-26.9	57.7	1253.8
S.D.		37.2	11.0	30.8	311.9
S.E.		11.8	3.5	9.7	98.6
N		10	10	10	10
WEEK 8	MEAN	72.	NA	NA	86.
% DIFFERENCE					19.4
S.D.		25.8			77.9
S.E.		8.1			24.6
N		10			10
ASPARTATE TRANSFER (U/L)					
WEEK 4	MEAN	72.	72.	90.	416.**
% DIFFERENCE			0.0	25.0	477.8
S.D.		18.5	13.3	38.0	218.3
S.E.		5.8	4.2	12.0	69.0
N		10	10	10	10
WEEK 8	MEAN	107.	NA	NA	88.
% DIFFERENCE					-17.8
S.D.		21.3			21.2
S.E.		8.1			7.1
N		7			9

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PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 29 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 6

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
GLUCOSE (mg/dL)					
WEEK 4	MEAN	167.	183.	182.	144.
% DIFFERENCE			9.6	9.0	-13.8
S.D.		24.4	17.6	26.3	22.9
S.E.		8.1	5.6	8.3	7.3
N		9	10	10	10
WEEK 8	MEAN	153.	NA	NA	182.
% DIFFERENCE					19.0
S.D.		44.8			27.0
S.E.		16.9			9.0
N		7			9
CHOLESTEROL (mg/dL)					
WEEK 4	MEAN	147.	127.	110. **	131.
% DIFFERENCE			-13.6	-25.2	-10.9
S.D.		18.2	18.3	20.5	39.8
S.E.		5.8	5.8	6.5	12.6
N		10	10	10	10
WEEK 8	MEAN	155.	NA	NA	146.
% DIFFERENCE					-5.8
S.D.		21.0			31.4
S.E.		6.6			9.9
N		10			10

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PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 29 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 7

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
CALCIUM (mg/dL)					
WEEK 4	MEAN	9.9	9.9	9.8	10.3
% DIFFERENCE			0.0	-1.0	4.0
S.D.		0.18	0.33	0.43	0.72
S.E.		0.06	0.10	0.14	0.23
N		10	10	10	10
WEEK 8	MEAN	9.9	NA	NA	10.0
% DIFFERENCE					1.0
S.D.		0.40			0.32
S.E.		0.15			0.11
N		7			9
CHLORIDE (mEq/L)					
WEEK 4	MEAN	113.	112.	114.	112.*
% DIFFERENCE			-0.9	0.9	-0.9
S.D.		2.0	1.3	1.1	1.1
S.E.		0.6	0.4	0.4	0.4
N		10	10	9	9
WEEK 8	MEAN	111.	NA	NA	109.
% DIFFERENCE					-1.8
S.D.		1.8			2.1
S.E.		0.7			0.7
N		7			9

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PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 29 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 8

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
PHOSPHORUS (mg/dL)					
WEEK 4	MEAN	9.1	9.0	9.2	9.4
% DIFFERENCE			-1.1	1.1	3.3
S.D.		0.98	0.98	0.79	0.84
S.E.		0.33	0.31	0.25	0.28
N		9	10	10	9
WEEK 8	MEAN	9.5	NA	NA	9.2
% DIFFERENCE					-3.2
S.D.		0.88			0.76
S.E.		0.33			0.25
N		7			9
POTASSIUM (mEq/L)					
WEEK 4	MEAN	5.97	5.84	5.41	5.51
% DIFFERENCE			-2.2	-9.4	-7.7
S.D.		0.613	0.230	0.432	0.582
S.E.		0.194	0.073	0.144	0.194
N		10	10	9	9
WEEK 8	MEAN	7.21	NA	NA	7.09
% DIFFERENCE					-1.7
S.D.		0.699			0.508
S.E.		0.264			0.169
N		7			9

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None significantly different from control group

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 29 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 9

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	
SODIUM (mEq/L)					
WEEK 4	MEAN	154.	153.	154.	153.
% DIFFERENCE		-0.6	0.0	-0.6	
S.D.		1.7	1.1	1.0	1.5
S.E.		0.5	0.3	0.3	0.5
N		10	10	9	9
WEEK 8	MEAN	151.	NA	NA	151.
% DIFFERENCE					0.0
S.D.		1.9			0.9
S.E.		0.7			0.3
N		7			9
TRIGLYCERIDE (mg/dL)					
WEEK 4	MEAN	174.	175.	173.	165.
% DIFFERENCE		0.6	-0.6	-5.2	
S.D.		18.1	51.9	46.6	19.7
S.E.		5.7	16.4	14.7	6.2
N		10	10	10	10
WEEK 8	MEAN	161.	NA	NA	158.
% DIFFERENCE					-1.9
S.D.		24.6			45.3
S.E.		7.8			14.3
N		10			10

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None significantly different from control group

NA = NOT APPLICABLE

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04/21/2008

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 30 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 1

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
ALEBUMIN (g/dL)					
WEEK 4	MEAN	3.6	3.4	3.5	3.8*
% DIFFERENCE			-5.6	-2.8	5.6
S.D.		0.16	0.11	0.21	0.25
S.E.		0.05	0.03	0.07	0.08
N		10	10	10	10
WEEK 8	MEAN	3.2	NA	NA	3.1
% DIFFERENCE					-3.1
S.D.		0.26			0.33
S.E.		0.09			0.11
N		9			9
TOTAL PROTEIN (g/dL)					
WEEK 4	MEAN	5.4	5.2	5.2	5.3
% DIFFERENCE			-3.7	-3.7	-1.9
S.D.		0.23	0.22	0.31	0.32
S.E.		0.07	0.07	0.10	0.10
N		10	10	10	10
WEEK 8	MEAN	5.6	NA	NA	5.0
% DIFFERENCE					-10.7
S.D.		1.43			0.35
S.E.		0.48			0.12
N		9			9

mg/dL = MILLIGRAMS/DECILITER, U/L = INTERNATIONAL UNIT/LITER, g/dL = GRAMS/DECILITER, mEq/L = MILLIEQUIVALENTS/LITER

* = Significantly different from the control group at 0.05 using Dunnett's test
NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 30 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 2

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
GLOBULIN (g/dL)					
WEEK 4	MEAN	1.9	1.8	1.6**	1.5**
% DIFFERENCE			-5.3	-15.8	-21.1
S.D.		0.14	0.13	0.11	0.13
S.E.		0.04	0.04	0.03	0.04
N		10	10	10	10
WEEK 8	MEAN	2.4	NA	NA	1.9
% DIFFERENCE					-20.8
S.D.		1.40			0.45
S.E.		0.47			0.15
N		9			9
A/G RATIO					
WEEK 4	MEAN	1.93	1.98	2.20**	2.46**
% DIFFERENCE			2.6	14.0	27.5
S.D.		0.159	0.134	0.087	0.190
S.E.		0.050	0.042	0.028	0.060
N		10	10	10	10
WEEK 8	MEAN	1.64	NA	NA	1.75
% DIFFERENCE					6.7
S.D.		0.580			0.381
S.E.		0.193			0.127
N		9			9

mg/dL = MILLIGRAMS/DECILITER, U/L = INTERNATIONAL UNIT/LITER, g/dL = GRAMS/DECILITER, mEq/L = MILLIEQUIVALENTS/LITER

** = Significantly different from the control group at 0.01 using Dunnett's test

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 30 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 3

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>					
TOTAL BILI (mg/dL)					
WEEK 4	MEAN	0.1	0.1	0.1	0.1
% DIFFERENCE			0.0	0.0	0.0
S.D.		0.00	0.03	0.03	0.04
S.E.		0.00	0.01	0.01	0.01
N		10	10	10	10
WEEK 8	MEAN	0.1	NA	NA	0.1
% DIFFERENCE					0.0
S.D.		0.03			0.00
S.E.		0.01			0.00
N		9			9
UREA NITROGEN (mg/dL)					
WEEK 4	MEAN	21.7	19.3	24.6	22.0
% DIFFERENCE			-11.1	13.4	1.4
S.D.		3.75	3.12	11.08	3.87
S.E.		1.25	1.27	3.92	1.37
N		9	6	8	8
WEEK 8	MEAN	18.1	NA	NA	19.8
% DIFFERENCE					9.4
S.D.		3.64			2.64
S.E.		1.38			1.00
N		7			7

mg/dL = MILLIGRAMS/DECILITER, U/L = INTERNATIONAL UNIT/LITER, g/dL = GRAMS/DECILITER, mEq/L = MILLIEQUIVALENTS/LITER

None significantly different from control group

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 30 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 4

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
CREATININE (mg/dL)					
WEEK 4	MEAN	1.1	0.5	0.7	1.2
% DIFFERENCE			-54.5	-36.4	9.1
S.D.		1.57	0.54	1.08	1.52
S.E.		0.59	0.24	0.41	0.76
N		7	5	7	4
WEEK 8	MEAN	0.6	NA	NA	0.0
% DIFFERENCE					-100.0
S.D.		1.35			0.05
S.E.		0.55			0.03
N		6			4
ALKALINEPHOS/TSE (U/L)					
WEEK 4	MEAN	90.	97.	96.	216.**
% DIFFERENCE			7.8	6.7	140.0
S.D.		21.9	22.1	19.7	51.3
S.E.		6.9	7.0	6.2	16.2
N		10	10	10	10
WEEK 8	MEAN	64.	NA	NA	73.
% DIFFERENCE					14.1
S.D.		12.8			37.3
S.E.		4.3			12.4
N		9			9

mg/dL = MILLIGRAMS/DECILITER, U/L = INTERNATIONAL UNIT/LITER, g/dL = GRAMS/DECILITER, mEq/L = MILLIEQUIVALENTS/LITER

** = Significantly different from the control group at 0.01 using Dunnett's test

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 30 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 5

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>					
ALANINE TRANSFER (U/L)					
WEEK 4	MEAN	52.	38.	63.	83.
% DIFFERENCE			-26.9	21.2	59.6
S.D.		33.2	7.7	47.5	26.1
S.E.		10.5	2.4	15.0	8.3
N		10	10	10	10
WEEK 8	MEAN	40.	NA	NA	44.
% DIFFERENCE					10.0
S.D.		10.7			16.5
S.E.		3.6			5.5
N		9			9
<hr/>					
ASPARTATE TRANSFER (U/L)					
WEEK 4	MEAN	115.	113.	111.	117.
% DIFFERENCE			-1.7	-3.5	1.7
S.D.		41.6	43.2	40.2	33.0
S.E.		13.9	15.3	12.7	10.4
N		9	8	10	10
WEEK 8	MEAN	88.	NA	NA	87.
% DIFFERENCE					-1.1
S.D.		33.5			26.4
S.E.		12.7			10.0
N		7			7

mg/dL = MILLIGRAMS/DECILITER, U/L = INTERNATIONAL UNIT/LITER, g/dL = GRAMS/DECILITER, mEq/L = MILLIEQUIVALENTS/LITER

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 30 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 6

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
GLUCOSE (mg/dL)					
WEEK 4	MEAN	144.	140.	133.	138.
% DIFFERENCE			-2.8	-7.6	-4.2
S.D.		25.2	24.6	27.2	39.9
S.E.		9.5	10.1	8.6	13.3
N		7	6	10	9
WEEK 8	MEAN	150.	NA	NA	170.
% DIFFERENCE					13.3
S.D.		20.1			23.7
S.E.		7.6			8.9
N		7			7
CHOLESTEROL (mg/dL)					
WEEK 4	MEAN	107.	95.	125.	106.
% DIFFERENCE			-11.2	16.8	-0.9
S.D.		21.3	15.1	19.3	27.8
S.E.		6.7	4.8	6.1	8.8
N		10	10	10	10
WEEK 8	MEAN	84.	NA	NA	98.
% DIFFERENCE					16.7
S.D.		17.3			14.9
S.E.		5.8			5.0
N		9			9

mg/dL = MILLIGRAMS/DECILITER, U/L = INTERNATIONAL UNIT/LITER, g/dL = GRAMS/DECILITER, mEq/L = MILLIEQUIVALENTS/LITER

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 30 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 7

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>					
CALCIUM (mg/dL)					
WEEK 4	MEAN	11.6	10.8	10.3	10.2
% DIFFERENCE		-6.9	-11.2	-12.1	
S.D.		2.92	0.97	0.65	0.44
S.E.		0.92	0.34	0.20	0.18
N		10	8	10	6
WEEK 8	MEAN	9.6	NA	NA	9.5
% DIFFERENCE		-1.0			
S.D.		0.37			0.16
S.E.		0.14			0.06
N		7			7
CHLORIDE (mEq/L)					
WEEK 4	MEAN	114.	115.	116.	114.
% DIFFERENCE		0.9	1.8	0.0	
S.D.		1.5	1.7	2.8	2.1
S.E.		0.9	0.7	1.0	0.8
N		3	6	7	7
WEEK 8	MEAN	112.	NA	NA	113.
% DIFFERENCE		0.9			
S.D.		2.4			1.9
S.E.		0.9			0.7
N		7			7

mg/dL = MILLIGRAMS/DECILITER, U/L = INTERNATIONAL UNIT/LITER, g/dL = GRAMS/DECILITER, mEq/L = MILLIEQUIVALENTS/LITER

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 30 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 8

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
PHOSPHORUS (mg/dL)					
WEEK 4	MEAN	8.9	9.7	9.3	10.3
% DIFFERENCE			9.0	4.5	15.7
S.D.		0.70	1.14	1.32	1.15
S.E.		0.31	0.51	0.50	0.44
N		5	5	7	7
WEEK 8	MEAN	8.0	NA	NA	8.1
% DIFFERENCE					1.3
S.D.		0.93			1.01
S.E.		0.35			0.38
N		7			7
POTASSIUM (mEq/L)					
WEEK 4	MEAN	5.57	6.14	7.09	6.91
% DIFFERENCE			10.2	27.3	24.1
S.D.		0.158	0.443	2.146	2.379
S.E.		0.091	0.181	0.811	0.899
N		3	6	7	7
WEEK 8	MEAN	5.84	NA	NA	5.52
% DIFFERENCE					-5.5
S.D.		0.458			0.527
S.E.		0.173			0.199
N		7			7

mg/dL = MILLIGRAMS/DECILITER, U/L = INTERNATIONAL UNIT/LITER, g/dL = GRAMS/DECILITER, mEq/L = MILLIEQUIVALENTS/LITER

None significantly different from control group

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 30 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SERUM CHEMISTRY VALUES

PAGE 9

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
SODIUM (mEq/L)					
WEEK 4	MEAN	153.	155.	157.	155.
% DIFFERENCE			1.3	2.6	1.3
S.D.		3.5	3.2	4.3	4.1
S.E.		2.0	1.3	1.6	1.5
N		3	6	7	7
WEEK 8	MEAN	149.	NA	NA	150.
% DIFFERENCE					0.7
S.D.		2.2			1.5
S.E.		0.8			0.6
N		7			7
TRIGLYCERIDE (mg/dL)					
WEEK 4	MEAN	173.	168.	326.	150.
% DIFFERENCE			-2.9	88.4	-13.3
S.D.		31.5	31.1	534.2	15.5
S.E.		10.0	9.8	168.9	4.9
N		10	10	10	10
WEEK 8	MEAN	109.	NA	NA	131.
% DIFFERENCE					20.2
S.D.		26.2			33.6
S.E.		8.7			11.2
N		9			9

mg/dL = MILLIGRAMS/DECILITER, U/L = INTERNATIONAL UNIT/LITER, g/dL = GRAMS/DECILITER, mEq/L = MILLIEQUIVALENTS/LITER

None significantly different from control group

NA = NOT APPLICABLE

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PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 31 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SPECIAL CHEMISTRY VALUES

PAGE 1

ANALYSIS	GROUP:	MALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
SORBITOL'GENASE (U/L)					
WEEK 4	MEAN	24.	22.	46.	456.**
% DIFFERENCE			-8.3	91.7	1800.0
S.D.		5.4	3.4	20.4	225.2
S.E.		1.7	1.1	6.5	75.1
N		10	10	10	9
WEEK 8	MEAN	18.	NA	NA	25.*
% DIFFERENCE					38.9
S.D.		6.1			5.0
S.E.		1.9			1.6
N		10			10

U/L = INTERNATIONAL UNIT/LITER

* = Significantly different from the control group at 0.05 using Dunnett's test

** = Significantly different from the control group at 0.01 using Dunnett's test

NA = NOT APPLICABLE

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PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 32 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF SPECIAL CHEMISTRY VALUES

PAGE 1

ANALYSIS	GROUP:	FEMALES			
		0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
SORBITOL'GENASE (U/L)					
WEEK 4	MEAN	14.	16.	16.	40.**
% DIFFERENCE			14.3	14.3	185.7
S.D.		5.1	4.8	5.5	20.2
S.E.		1.6	1.5	1.7	6.4
N		10	10	10	10
WEEK 8	MEAN	12.	NA	NA	14.
% DIFFERENCE					16.7
S.D.		4.4			5.2
S.E.		1.5			1.7
N		8			9

U/L = INTERNATIONAL UNIT/LITER

** = Significantly different from the control group at 0.01 using Dunnett's test

NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 33 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MACROSCOPIC FINDINGS

PAGE 1

FOUND DEAD OR EUTHANIZED MORIBUND OR IN EXTREMIS

GROUP:	F E M A L E			
	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	1	0	0	1
NO SIGNIFICANT CHANGES OBSERVED - ALL EXAMINED TISSUES	1	0	0	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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WIL-189207

PROJECT NO.: WIL-189207M
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SPONSOR NO.: DUPONT-24459

TABLE 34 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MACROSCOPIC FINDINGS

PAGE 1

SCHEDULED NECROPSY

GROUP:	MALES			
	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
ADRENAL GLANDS				
-SMALL	0	1	0	0
ESOPHAGUS				
-NODULE(S)	0	0	0	1
KIDNEYS				
-CYST(S)	0	0	0	1
LIVER				
-ENLARGED	0	0	0	7
-AREA(S), WHITE	0	0	0	1
LYMPH NODE, MAND				
-ENLARGED	0	0	1	0
NO SIGNIFICANT CHANGES OBSERVED - ALL EXAMINED TISSUES	10	9	9	3

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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04/21/2008

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 35 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MACROSCOPIC FINDINGS

PAGE 1

SCHEDULED NECROPSY

GROUP:	F E M A L E			
	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
EYES/OPTIC N.				
-EYE(S)- OPACITY	1	1	1	0
OVARIES				
-CYST(S)	1	1	1	0
OVIDUCTS				
-CYST(S)	1	0	1	1
PAWS				
-DIGIT(S)- MISSING	1	0	0	0
SPLEEN				
-ACCESSORY	2	1	0	0
TAIL				
-SCABBING	1	0	1	0
UTERUS				
-CONTENTS, CLEAR FLUID	2	0	1	0
NO SIGNIFICANT CHANGES OBSERVED - ALL EXAMINED TISSUES	5	7	7	9

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 36 (WEEK 8 RECOVERY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MACROSCOPIC FINDINGS

PAGE 1

SCHEDULED NECROPSY

	GROUP:	1	M A L E	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20		10		
NUMBER OF ANIMALS EXAMINED		10		0		
KIDNEYS						
-CYST(S)		0		0		
LYMPH NODE, MAND						
-ENLARGED		1		0		
TESTES						
-SMALL		0		0		
-SOFT		0		0		
NO SIGNIFICANT CHANGES OBSERVED - ALL EXAMINED TISSUES		9		0		
	9			0		
	7			0		

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 37 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MACROSCOPIC FINDINGS

PAGE 1

SCHEDULED NECROPSY

GROUP:	F E M A L E				PAGE
	1	2	3	4	
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20	
NUMBER OF ANIMALS EXAMINED	9	0	0	9	
ADIPOSE TISSUE					
-MASS	1	0	0	0	
ESOPHAGUS					
-MASS	0	0	0	1	
LYMPH NODE, BRON					
-ENLARGED	1	0	0	1	
LYMPH NODE, GEN					
-ENLARGED	1	0	0	1	
LYMPH NODE, MAND					
-ENLARGED	1	0	0	1	
LYMPH NODE, MED					
-ENLARGED	1	0	0	1	
MAMMARY GLAND					
-MASS	0	0	0	1	
OVARIES					
-CYST(S)	1	0	0	2	
SKIN					
-MASS	0	0	0	1	

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 37 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MACROSCOPIC FINDINGS

PAGE 2

SCHEDULED NECROPSY

GROUP:	F E M A L E			
	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	9	0	0	9
SPLEEN -ENLARGED	0	0	0	1
TAIL -FRACTURED	1	0	0	0
UTERUS -CONTENTS, CLEAR FLUID	0	0	0	1
NO SIGNIFICANT CHANGES OBSERVED - ALL EXAMINED TISSUES	6	0	0	6

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

PGRSI2v4.07
04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 38 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 1

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
FINAL BODY WT (G)				
MEAN	35.0	34.2	34.5	35.4
% DIFFERENCE		-2.3	-1.4	1.1
S.D.	2.78	2.38	2.75	2.99
S.E.	0.88	0.75	0.87	0.95
N	10	10	10	10
ADRENAL GLANDS (G)				
MEAN	0.0046	0.0045	0.0059	0.0075**
% DIFFERENCE		-2.2	28.3	63.0
S.D.	0.00101	0.00176	0.00092	0.00177
S.E.	0.00032	0.00056	0.00029	0.00056
N	10	10	10	10
ADRENAL GLANDS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.013	0.013	0.017	0.022**
% DIFFERENCE		0.0	30.8	69.2
S.D.	0.0030	0.0058	0.0032	0.0065
S.E.	0.0009	0.0018	0.0010	0.0020
N	10	10	10	10
ADRENAL GLANDS (G/100 G BRAIN)				
MEAN	0.950	0.915	1.215	1.561**
% DIFFERENCE		-3.7	27.9	64.3
S.D.	0.1895	0.3706	0.1869	0.3172
S.E.	0.0599	0.1172	0.0591	0.1003
N	10	10	10	10

** = Significantly different from the control group at 0.01 using Dunnett's test

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 38 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 2

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
BRAIN (G)				
MEAN	0.4852	0.4938	0.4846	0.4767
% DIFFERENCE		1.8	-0.1	-1.8
S.D.	0.02743	0.01682	0.01394	0.02090
S.E.	0.00867	0.00532	0.00441	0.00661
N	10	10	10	10
BRAIN (G/100 G FINAL BODY WEIGHT)				
MEAN	1.390	1.451	1.414	1.360
% DIFFERENCE		4.4	1.7	-2.2
S.D.	0.0729	0.0923	0.1042	0.1581
S.E.	0.0231	0.0292	0.0330	0.0500
N	10	10	10	10
EPIDIDYMIDES (G)				
MEAN	0.0920	0.0935	0.0831	0.0898
% DIFFERENCE		1.6	-9.7	-2.4
S.D.	0.01332	0.01141	0.01161	0.01259
S.E.	0.00421	0.00361	0.00367	0.00398
N	10	10	10	10
EPIDIDYMIDES (G/100 G FINAL BODY WEIGHT)				
MEAN	0.262	0.276	0.242	0.256
% DIFFERENCE		5.3	-7.6	-2.3
S.D.	0.0268	0.0492	0.0344	0.0450
S.E.	0.0085	0.0156	0.0109	0.0142
N	10	10	10	10

None significantly different from control group

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 38 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 3

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
EPIDIDYMIDES (G/100 G BRAIN)				
MEAN	18.910	18.995	17.126	18.829
% DIFFERENCE		0.4	-9.4	-0.4
S.D.	2.0005	2.7548	2.1721	2.4360
S.E.	0.6326	0.8712	0.6869	0.7703
N	10	10	10	10
HEART (G)				
MEAN	0.1807	0.1767	0.1762	0.1751
% DIFFERENCE		-2.2	-2.5	-3.1
S.D.	0.02848	0.00862	0.02358	0.01771
S.E.	0.00900	0.00273	0.00746	0.00560
N	10	10	10	10
HEART (G/100 G FINAL BODY WEIGHT)				
MEAN	0.518	0.519	0.511	0.497
% DIFFERENCE		0.2	-1.4	-4.1
S.D.	0.0792	0.0398	0.0509	0.0555
S.E.	0.0250	0.0126	0.0161	0.0175
N	10	10	10	10
HEART (G/100 G BRAIN)				
MEAN	37.277	35.788	36.410	36.768
% DIFFERENCE		-4.0	-2.3	-1.4
S.D.	5.6479	1.5090	5.2505	3.7746
S.E.	1.7860	0.4772	1.6603	1.1936
N	10	10	10	10

None significantly different from control group

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 38 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 4

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
KIDNEYS (G)				
MEAN	0.5567	0.5621	0.5309	0.5735
% DIFFERENCE		1.0	-4.6	3.0
S.D.	0.06728	0.06191	0.04847	0.07030
S.E.	0.02128	0.01958	0.01533	0.02223
N	10	10	10	10
KIDNEYS (G/100 G FINAL BODY WEIGHT)				
MEAN	1.590	1.649	1.543	1.622
% DIFFERENCE		3.7	-3.0	2.0
S.D.	0.1396	0.1682	0.0978	0.1347
S.E.	0.0442	0.0532	0.0309	0.0426
N	10	10	10	10
KIDNEYS (G/100 G BRAIN)				
MEAN	114.622	113.858	109.586	120.516
% DIFFERENCE		-0.7	-4.4	5.1
S.D.	10.6419	12.1439	9.8970	15.4572
S.E.	3.3653	3.8402	3.1297	4.8880
N	10	10	10	10
LIVER (G)				
MEAN	1.6907	1.8046	2.9609**	4.5021**
% DIFFERENCE		6.7	75.1	166.3
S.D.	0.24208	0.19656	0.55030	0.87032
S.E.	0.07655	0.06216	0.17402	0.27522
N	10	10	10	10

** = Significantly different from the control group at 0.01 using Dunnett's test

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 38 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 5

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
LIVER (G/100 G FINAL BODY WEIGHT)				
MEAN	4.816	5.282	8.555**	12.669**
% DIFFERENCE		9.7	77.6	163.1
S.D.	0.4493	0.3908	1.0672	1.8178
S.E.	0.1421	0.1236	0.3375	0.5749
N	10	10	10	10
LIVER (G/100 G BRAIN)				
MEAN	347.314	365.446	611.951**	948.956**
% DIFFERENCE		5.2	76.2	173.2
S.D.	35.9339	37.5748	119.6603	204.0532
S.E.	11.3633	11.8822	37.8399	64.5273
N	10	10	10	10
SPLEEN (G)				
MEAN	0.0952	0.0872	0.0813	0.0956
% DIFFERENCE		-8.4	-14.6	0.4
S.D.	0.02074	0.01579	0.02832	0.02266
S.E.	0.00656	0.00499	0.00896	0.00716
N	10	10	10	10
SPLEEN (G/100 G FINAL BODY WEIGHT)				
MEAN	0.271	0.256	0.234	0.269
% DIFFERENCE		-5.5	-13.7	-0.7
S.D.	0.0518	0.0465	0.0693	0.0508
S.E.	0.0164	0.0147	0.0219	0.0161
N	10	10	10	10

** = Significantly different from the control group at 0.01 using Dunnett's test

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 38 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 6

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
SPLEEN (G/100 G BRAIN)				
MEAN	19.554	17.644	16.823	20.103
% DIFFERENCE		-9.8	-14.0	2.8
S.D.	3.7645	3.0592	6.0804	4.8433
S.E.	1.1904	0.9674	1.9228	1.5316
N	10	10	10	10
TESTES (G)				
MEAN	0.2366	0.2331	0.2228	0.2093
% DIFFERENCE		-1.5	-5.8	-11.5
S.D.	0.04067	0.01744	0.03276	0.01863
S.E.	0.01286	0.00552	0.01036	0.00589
N	10	10	10	10
TESTES (G/100 G FINAL BODY WEIGHT)				
MEAN	0.674	0.687	0.647	0.595
% DIFFERENCE		1.9	-4.0	-11.7
S.D.	0.0920	0.0855	0.0769	0.0648
S.E.	0.0291	0.0270	0.0243	0.0205
N	10	10	10	10
TESTES (G/100 G BRAIN)				
MEAN	48.571	47.302	45.895	43.995
% DIFFERENCE		-2.6	-5.5	-9.4
S.D.	6.9960	4.4101	5.8351	4.5823
S.E.	2.2123	1.3946	1.8452	1.4490
N	10	10	10	10

None significantly different from control group

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 38 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 7

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
THYMUS (G)				
MEAN	0.0401	0.0364	0.0338	0.0386
% DIFFERENCE		-9.2	-15.7	-3.7
S.D.	0.01174	0.00984	0.01762	0.00454
S.E.	0.00371	0.00311	0.00557	0.00144
N	10	10	10	10
THYMUS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.114	0.108	0.098	0.109
% DIFFERENCE		-5.3	-14.0	-4.4
S.D.	0.0292	0.0322	0.0489	0.0115
S.E.	0.0092	0.0102	0.0155	0.0037
N	10	10	10	10
THYMUS (G/100 G BRAIN)				
MEAN	8.236	7.391	6.961	8.132
% DIFFERENCE		-10.3	-15.5	-1.3
S.D.	2.2571	2.0392	3.5371	1.1273
S.E.	0.7138	0.6448	1.1185	0.3565
N	10	10	10	10

None significantly different from control group

POFBSTv5.11
04/21/2008

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 39 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 1

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
FINAL BODY WT (G)				
MEAN	26.6	27.3	27.0	27.3
% DIFFERENCE		2.6	1.5	2.6
S.D.	1.84	1.32	1.70	1.59
S.E.	0.58	0.42	0.54	0.50
N	10	10	10	10
ADRENAL GLANDS (G)				
MEAN	0.0103	0.0105	0.0094	0.0107
% DIFFERENCE		1.9	-8.7	3.9
S.D.	0.00234	0.00229	0.00201	0.00284
S.E.	0.00074	0.00073	0.00064	0.00090
N	10	10	10	10
ADRENAL GLANDS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.039	0.039	0.035	0.039
% DIFFERENCE		0.0	-10.3	0.0
S.D.	0.0105	0.0088	0.0068	0.0090
S.E.	0.0033	0.0028	0.0021	0.0029
N	10	10	10	10
ADRENAL GLANDS (G/100 G BRAIN)				
MEAN	2.185	2.136	1.932	2.219
% DIFFERENCE		-2.2	-11.6	1.6
S.D.	0.5526	0.4948	0.5084	0.5134
S.E.	0.1747	0.1565	0.1608	0.1624
N	10	10	10	10

None significantly different from control group

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 39 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 2

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
BRAIN (G)				
MEAN	0.4711	0.4946	0.4923	0.4772
% DIFFERENCE		5.0	4.5	1.3
S.D.	0.02665	0.01711	0.03403	0.02780
S.E.	0.00843	0.00541	0.01076	0.00879
N	10	10	10	10
BRAIN (G/100 G FINAL BODY WEIGHT)				
MEAN	1.776	1.816	1.823	1.750
% DIFFERENCE		2.3	2.6	-1.5
S.D.	0.1085	0.1193	0.1009	0.0797
S.E.	0.0343	0.0377	0.0319	0.0252
N	10	10	10	10
HEART (G)				
MEAN	0.1333	0.1492	0.1437	0.1451
% DIFFERENCE		11.9	7.8	8.9
S.D.	0.01638	0.01874	0.01623	0.02155
S.E.	0.00518	0.00593	0.00513	0.00681
N	10	10	10	10
HEART (G/100 G FINAL BODY WEIGHT)				
MEAN	0.502	0.548	0.534	0.532
% DIFFERENCE		9.2	6.4	6.0
S.D.	0.0650	0.0734	0.0692	0.0748
S.E.	0.0206	0.0232	0.0219	0.0236
N	10	10	10	10

None significantly different from control group

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 39 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 3

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
HEART (G/100 G BRAIN)				
MEAN	28.367	30.161	29.256	30.437
% DIFFERENCE		6.3	3.1	7.3
S.D.	4.0567	3.5773	3.2981	4.4385
S.E.	1.2828	1.1312	1.0429	1.4036
N	10	10	10	10
KIDNEYS (G)				
MEAN	0.3348	0.3717*	0.3521	0.4038**
% DIFFERENCE		11.0	5.2	20.6
S.D.	0.03570	0.01943	0.02851	0.03444
S.E.	0.01129	0.00614	0.00902	0.01089
N	10	10	10	10
KIDNEYS (G/100 G FINAL BODY WEIGHT)				
MEAN	1.259	1.364*	1.303	1.478**
% DIFFERENCE		8.3	3.5	17.4
S.D.	0.0989	0.0930	0.0808	0.0746
S.E.	0.0313	0.0294	0.0256	0.0236
N	10	10	10	10
KIDNEYS (G/100 G BRAIN)				
MEAN	70.988	75.148	71.590	84.553**
% DIFFERENCE		5.9	0.8	19.1
S.D.	5.5906	2.9615	4.2751	4.0094
S.E.	1.7679	0.9365	1.3519	1.2679
N	10	10	10	10

* = Significantly different from the control group at 0.05 using Dunnett's test

** = Significantly different from the control group at 0.01 using Dunnett's test

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 39 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 4

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
LIVER (G)				
MEAN	1.2765	1.4100	1.7115**	2.6570**
% DIFFERENCE		10.5	34.1	108.1
S.D.	0.17847	0.13589	0.23249	0.43326
S.E.	0.05644	0.04297	0.07352	0.13701
N	10	10	10	10
LIVER (G/100 G FINAL BODY WEIGHT)				
MEAN	4.785	5.156	6.321**	9.699**
% DIFFERENCE		7.8	32.1	102.7
S.D.	0.4267	0.3002	0.6333	1.2157
S.E.	0.1349	0.0949	0.2003	0.3845
N	10	10	10	10
LIVER (G/100 G BRAIN)				
MEAN	270.582	285.470	347.618**	554.315**
% DIFFERENCE		5.5	28.5	104.9
S.D.	31.8333	29.7700	38.6819	65.5015
S.E.	10.0666	9.4141	12.2323	20.7134
N	10	10	10	10
OVARIES/OVIDUCTS (G)				
MEAN	0.0256	0.0275	0.0252	0.0276
% DIFFERENCE		7.4	-1.6	7.8
S.D.	0.00328	0.00780	0.00333	0.00994
S.E.	0.00104	0.00247	0.00105	0.00314
N	10	10	10	10

** = Significantly different from the control group at 0.01 using Dunnett's test

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 39 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 5

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
OVARIES/OVIDUCTS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.096	0.100	0.093	0.101
% DIFFERENCE		4.2	-3.1	5.2
S.D.	0.0113	0.0277	0.0125	0.0358
S.E.	0.0036	0.0088	0.0040	0.0113
N	10	10	10	10
OVARIES/OVIDUCTS (G/100 G BRAIN)				
MEAN	5.440	5.579	5.122	5.739
% DIFFERENCE		2.6	-5.8	5.5
S.D.	0.7080	1.6753	0.6358	1.8721
S.E.	0.2239	0.5298	0.2011	0.5920
N	10	10	10	10
SPLEEN (G)				
MEAN	0.0868	0.1105*	0.0828	0.0858
% DIFFERENCE		27.3	-4.6	-1.2
S.D.	0.01979	0.03052	0.01396	0.01152
S.E.	0.00626	0.00965	0.00441	0.00364
N	10	10	10	10
SPLEEN (G/100 G FINAL BODY WEIGHT)				
MEAN	0.326	0.403*	0.305	0.314
% DIFFERENCE		23.6	-6.4	-3.7
S.D.	0.0679	0.1005	0.0384	0.0364
S.E.	0.0215	0.0318	0.0122	0.0115
N	10	10	10	10

* = Significantly different from the control group at 0.05 using Dunnett's test

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 39 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 6

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
SPLEEN (G/100 G BRAIN)				
MEAN	18.458	22.359	16.808	18.009
% DIFFERENCE		21.1	-8.9	-2.4
S.D.	4.3988	6.1531	2.4592	2.4914
S.E.	1.3910	1.9458	0.7777	0.7879
N	10	10	10	10
THYMUS (G)				
MEAN	0.0455	0.0486	0.0389	0.0401
% DIFFERENCE		6.8	-14.5	-11.9
S.D.	0.01241	0.00894	0.00562	0.00766
S.E.	0.00392	0.00283	0.00178	0.00242
N	10	10	10	10
THYMUS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.172	0.178	0.144	0.147
% DIFFERENCE		3.5	-16.3	-14.5
S.D.	0.0464	0.0349	0.0208	0.0285
S.E.	0.0147	0.0110	0.0066	0.0090
N	10	10	10	10
THYMUS (G/100 G BRAIN)				
MEAN	9.714	9.825	7.903	8.429
% DIFFERENCE		1.1	-18.6	-13.2
S.D.	2.7799	1.8482	0.9945	1.6382
S.E.	0.8791	0.5845	0.3145	0.5180
N	10	10	10	10

None significantly different from control group

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 39 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 7

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
UTERUS (G)				
MEAN	0.1807	0.1548	0.1579	0.1101*
% DIFFERENCE		-14.3	-12.6	-39.1
S.D.	0.05967	0.06753	0.05248	0.02580
S.E.	0.01887	0.02136	0.01660	0.00816
N	10	10	10	10
UTERUS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.681	0.562	0.588	0.405**
% DIFFERENCE		-17.5	-13.7	-40.5
S.D.	0.2206	0.2247	0.2006	0.0985
S.E.	0.0698	0.0711	0.0634	0.0311
N	10	10	10	10
UTERUS (G/100 G BRAIN)				
MEAN	38.595	31.328	32.515	23.042*
% DIFFERENCE		-18.8	-15.8	-40.3
S.D.	13.4197	13.6494	11.7030	5.2689
S.E.	4.2437	4.3163	3.7008	1.6662
N	10	10	10	10

* = Significantly different from the control group at 0.05 using Dunnett's test

** = Significantly different from the control group at 0.01 using Dunnett's test

POFBSTv5.11
04/21/2008

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 40 (WEEK 8 RECOVERY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 1

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
FINAL BODY WT (G)				
MEAN	38.6	NA	NA	38.0
% DIFFERENCE				-1.6
S.D.	3.36			4.04
S.E.	1.06			1.28
N	10			10
ADRENAL GLANDS (G)				
MEAN	0.0047	NA	NA	0.0053
% DIFFERENCE				12.8
S.D.	0.00107			0.00107
S.E.	0.00034			0.00034
N	10			10
ADRENAL GLANDS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.012	NA	NA	0.014
% DIFFERENCE				16.7
S.D.	0.0035			0.0027
S.E.	0.0011			0.0009
N	10			10
ADRENAL GLANDS (G/100 G BRAIN)				
MEAN	0.962	NA	NA	1.098
% DIFFERENCE				14.1
S.D.	0.2333			0.2446
S.E.	0.0738			0.0774
N	10			10

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 40 (WEEK 8 RECOVERY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 2

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
BRAIN (G)				
MEAN	0.4945	NA	NA	0.4885
% DIFFERENCE				-1.2
S.D.	0.02216			0.02372
S.E.	0.00701			0.00750
N	10			10
BRAIN (G/100 G FINAL BODY WEIGHT)				
MEAN	1.288	NA	NA	1.298
% DIFFERENCE				0.8
S.D.	0.0904			0.1327
S.E.	0.0286			0.0420
N	10			10
EPIDIDYMIDES (G)				
MEAN	0.1038	NA	NA	0.0978
% DIFFERENCE				-5.8
S.D.	0.00597			0.01510
S.E.	0.00189			0.00478
N	10			10
EPIDIDYMIDES (G/100 G FINAL BODY WEIGHT)				
MEAN	0.271	NA	NA	0.259
% DIFFERENCE				-4.4
S.D.	0.0331			0.0400
S.E.	0.0105			0.0127
N	10			10

None significantly different from control group
NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 40 (WEEK 8 RECOVERY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 3

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
EPIDIDYMIDES (G/100 G BRAIN)				
MEAN	21.027		NA	
% DIFFERENCE			NA	
S.D.	1.5789			-4.8
S.E.	0.4993			3.0306
N	10			0.9584
				10
HEART (G)				
MEAN	0.1884		NA	
% DIFFERENCE			NA	
S.D.	0.02419			-3.1
S.E.	0.00765			0.01646
N	10			0.00521
				10
HEART (G/100 G FINAL BODY WEIGHT)				
MEAN	0.489		NA	
% DIFFERENCE			NA	
S.D.	0.0586			-1.2
S.E.	0.0185			0.0362
N	10			0.0114
				10
HEART (G/100 G BRAIN)				
MEAN	38.031		NA	
% DIFFERENCE			NA	
S.D.	3.9939			-1.6
S.E.	1.2630			3.1390
N	10			0.9926
				10

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 40 (WEEK 8 RECOVERY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 4

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
KIDNEYS (G)				
MEAN	0.6085	NA	NA	0.5819
% DIFFERENCE				-4.4
S.D.	0.06031			0.09922
S.E.	0.01907			0.03138
N	10			10
KIDNEYS (G/100 G FINAL BODY WEIGHT)				
MEAN	1.580	NA	NA	1.538
% DIFFERENCE				-2.7
S.D.	0.1371			0.2301
S.E.	0.0433			0.0728
N	10			10
KIDNEYS (G/100 G BRAIN)				
MEAN	123.062	NA	NA	119.273
% DIFFERENCE				-3.1
S.D.	11.4429			20.2516
S.E.	3.6185			6.4041
N	10			10
LIVER (G)				
MEAN	1.9127	NA	NA	2.3140*
% DIFFERENCE				21.0
S.D.	0.17584			0.54789
S.E.	0.05561			0.17326
N	10			10

* = Significantly different from the control group at 0.05 using Dunnett's test

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 40 (WEEK 8 RECOVERY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 5

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
LIVER (G/100 G FINAL BODY WEIGHT)				
MEAN	4.966	NA	NA	6.035** 21.5
% DIFFERENCE				0.9227
S.D.	0.3361			0.2918
S.E.	0.1063			10
N	10			
LIVER (G/100 G BRAIN)				
MEAN	387.159	NA	NA	471.570* 21.8
% DIFFERENCE				97.3797
S.D.	35.3445			30.7942
S.E.	11.1769			10
N	10			
SPLEEN (G)				
MEAN	0.0937	NA	NA	0.1050 12.1
% DIFFERENCE				0.02437
S.D.	0.01363			0.00771
S.E.	0.00431			10
N	10			
SPLEEN (G/100 G FINAL BODY WEIGHT)				
MEAN	0.243	NA	NA	0.278 14.4
% DIFFERENCE				0.0653
S.D.	0.0260			0.0206
S.E.	0.0082			10
N	10			

* = Significantly different from the control group at 0.05 using Dunnett's test

** = Significantly different from the control group at 0.01 using Dunnett's test

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 40 (WEEK 8 RECOVERY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 6

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
SPLEEN (G/100 G BRAIN)				
MEAN	18.949	NA	NA	21.414
% DIFFERENCE				13.0
S.D.	2.5494			4.3700
S.E.	0.8062			1.3819
N	10			10
TESTES (G)				
MEAN	0.2494	NA	NA	0.2233
% DIFFERENCE				-10.5
S.D.	0.03054			0.05011
S.E.	0.00966			0.01585
N	10			10
TESTES (G/100 G FINAL BODY WEIGHT)				
MEAN	0.647	NA	NA	0.595
% DIFFERENCE				-8.0
S.D.	0.0643			0.1474
S.E.	0.0203			0.0466
N	10			10
TESTES (G/100 G BRAIN)				
MEAN	50.387	NA	NA	45.757
% DIFFERENCE				-9.2
S.D.	5.4553			10.3129
S.E.	1.7251			3.2612
N	10			10

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 40 (WEEK 8 RECOVERY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 7

GROUP:	MALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
THYMUS (G)				
MEAN	0.0382	NA	NA	0.0369
% DIFFERENCE				-3.4
S.D.	0.01124			0.01390
S.E.	0.00355			0.00440
N	10			10
THYMUS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.099	NA	NA	0.097
% DIFFERENCE				-2.0
S.D.	0.0299			0.0330
S.E.	0.0095			0.0104
N	10			10
THYMUS (G/100 G BRAIN)				
MEAN	7.752	NA	NA	7.606
% DIFFERENCE				-1.9
S.D.	2.4356			2.9593
S.E.	0.7702			0.9358
N	10			10

None significantly different from control group
NA = NOT APPLICABLE

POFBSTv5.11
04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 41 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 1

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
FINAL BODY WT (G)				
MEAN	28.5	NA	NA	29.6
% DIFFERENCE				3.9
S.D.	1.90			3.10
S.E.	0.63			1.03
N	9			9
ADRENAL GLANDS (G)				
MEAN	0.0081	NA	NA	0.0098*
% DIFFERENCE				21.0
S.D.	0.00119			0.00185
S.E.	0.00040			0.00062
N	9			9
ADRENAL GLANDS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.028	NA	NA	0.034
% DIFFERENCE				21.4
S.D.	0.0038			0.0078
S.E.	0.0013			0.0026
N	9			9
ADRENAL GLANDS (G/100 G BRAIN)				
MEAN	1.673	NA	NA	2.022*
% DIFFERENCE				20.9
S.D.	0.2262			0.4327
S.E.	0.0754			0.1442
N	9			9

* = Significantly different from the control group at 0.05 using Dunnett's test

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 41 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 2

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
BRAIN (G)				
MEAN	0.4810	NA	NA	0.4870
% DIFFERENCE				1.2
S.D.	0.02056			0.03566
S.E.	0.00685			0.01189
N	9			9
BRAIN (G/100 G FINAL BODY WEIGHT)				
MEAN	1.693	NA	NA	1.658
% DIFFERENCE				-2.1
S.D.	0.0944			0.1822
S.E.	0.0315			0.0607
N	9			9
HEART (G)				
MEAN	0.1394	NA	NA	0.1461
% DIFFERENCE				4.8
S.D.	0.01581			0.01335
S.E.	0.00527			0.00445
N	9			9
HEART (G/100 G FINAL BODY WEIGHT)				
MEAN	0.490	NA	NA	0.495
% DIFFERENCE				1.0
S.D.	0.0488			0.0311
S.E.	0.0163			0.0104
N	9			9

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 41 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 3

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
HEART (G/100 G BRAIN)				
MEAN	29.006	NA	NA	30.081
% DIFFERENCE				3.7
S.D.	3.2674			2.7813
S.E.	1.0891			0.9271
N	9			9
KIDNEYS (G)				
MEAN	0.3699	NA	NA	0.4003
% DIFFERENCE				8.2
S.D.	0.04848			0.05016
S.E.	0.01616			0.01672
N	9			9
KIDNEYS (G/100 G FINAL BODY WEIGHT)				
MEAN	1.298	NA	NA	1.354
% DIFFERENCE				4.3
S.D.	0.1364			0.1081
S.E.	0.0455			0.0360
N	9			9
KIDNEYS (G/100 G BRAIN)				
MEAN	76.784	NA	NA	82.581
% DIFFERENCE				7.5
S.D.	8.4627			11.8769
S.E.	2.8209			3.9590
N	9			9

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 41 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 4

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
LIVER (G)				
MEAN	1.3623	NA	NA	1.6354
% DIFFERENCE				20.0
S.D.	0.19186			0.39949
S.E.	0.06395			0.13316
N	9			9
LIVER (G/100 G FINAL BODY WEIGHT)				
MEAN	4.787	NA	NA	5.473*
% DIFFERENCE				14.3
S.D.	0.6245			0.7008
S.E.	0.2082			0.2336
N	9			9
LIVER (G/100 G BRAIN)				
MEAN	283.683	NA	NA	336.726
% DIFFERENCE				18.7
S.D.	41.8371			80.1349
S.E.	13.9457			26.7116
N	9			9
OVARIES/OVIDUCTS (G)				
MEAN	0.0281	NA	NA	0.0290
% DIFFERENCE				3.2
S.D.	0.00893			0.00837
S.E.	0.00298			0.00279
N	9			9

* = Significantly different from the control group at 0.05 using Dunnett's test

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 41 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 5

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
OVARIES/OVIDUCTS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.098		NA	NA
% DIFFERENCE				
S.D.	0.0284			0.099
S.E.	0.0095			1.0
N	9			0.0339
				0.0113
				9
OVARIES/OVIDUCTS (G/100 G BRAIN)	5.812		NA	NA
MEAN				5.946
% DIFFERENCE				2.3
S.D.	1.7242			1.5757
S.E.	0.5747			0.5252
N	9			9
SPLEEN (G)				
MEAN	0.1113		NA	NA
% DIFFERENCE				
S.D.	0.04413			0.1563
S.E.	0.01471			40.4
N	9			0.15843
				0.05281
				9
SPLEEN (G/100 G FINAL BODY WEIGHT)	0.399		NA	NA
MEAN				0.496
% DIFFERENCE				24.3
S.D.	0.1945			0.4114
S.E.	0.0648			0.1371
N	9			9

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 41 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 6

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
<hr/>				
SPLEEN (G/100 G BRAIN)				
MEAN	23.360		NA	NA
% DIFFERENCE				32.108
S.D.	10.1563			37.4
S.E.	3.3854			31.5779
N	9			10.5260
				9
THYMUS (G)				
MEAN	0.0324		NA	0.0386
% DIFFERENCE				19.1
S.D.	0.01066			0.01813
S.E.	0.00355			0.00604
N	9			9
THYMUS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.113		NA	0.129
% DIFFERENCE				14.2
S.D.	0.0350			0.0568
S.E.	0.0117			0.0189
N	9			9
THYMUS (G/100 G BRAIN)				
MEAN	6.670		NA	7.925
% DIFFERENCE				18.8
S.D.	1.9589			3.5859
S.E.	0.6530			1.1953
N	9			9

None significantly different from control group

NA = NOT APPLICABLE

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 41 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF ORGAN WEIGHTS AND RELATIVE ORGAN WEIGHTS

PAGE 7

GROUP:	FEMALES			
	0 MG/KG/DAY	0.1 MG/KG/DAY	3 MG/KG/DAY	30 MG/KG/DAY
UTERUS (G)				
MEAN	0.1488	NA	NA	0.1534
% DIFFERENCE				3.1
S.D.	0.06043			0.05142
S.E.	0.02014			0.01714
N	9			9
UTERUS (G/100 G FINAL BODY WEIGHT)				
MEAN	0.521	NA	NA	0.514
% DIFFERENCE				-1.3
S.D.	0.2035			0.1396
S.E.	0.0678			0.0465
N	9			9
UTERUS (G/100 G BRAIN)				
MEAN	30.654	NA	NA	31.480
% DIFFERENCE				2.7
S.D.	11.4743			9.9588
S.E.	3.8248			3.3196
N	9			9

None significantly different from control group
NA = NOT APPLICABLE

POFBSTv5.11
04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 1

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	1	0	0	1
ADRENAL CORTEX				
TOTAL NUMBER EXAMINED	1	0	0	0
EXAMINED, UNREMARKABLE	0	0	0	0
-CONGESTION	1	0	0	0
MINIMAL	1	0	0	0
MILD	NONE	NONE	NONE	NONE
ADRENAL MEDULLA				
TOTAL NUMBER EXAMINED	1	0	0	0
EXAMINED, UNREMARKABLE	1	0	0	0
AORTA				
TOTAL NUMBER EXAMINED	1	0	0	0
EXAMINED, UNREMARKABLE	1	0	0	0
BRAIN				
TOTAL NUMBER EXAMINED	1	0	0	0
EXAMINED, UNREMARKABLE	1	0	0	0
CECUM				
TOTAL NUMBER EXAMINED	0	0	0	0
EXAMINED, UNREMARKABLE	0	0	0	0
TOO AUTOLYZED TO EXAMINE	1	0	0	0

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 2

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	1	0	0	1
CERVIX				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	0	0	0	0
-LUMINAL DEBRIS, CELLULAR	1	0	0	1
MILD	1	NONE	NONE	1
COLON				
TOTAL NUMBER EXAMINED	0	0	0	1
EXAMINED, UNREMARKABLE	0	0	0	1
TOO AUTOLYZED TO EXAMINE	1	0	0	0
DUODENUM				
TOTAL NUMBER EXAMINED	0	0	0	1
EXAMINED, UNREMARKABLE	0	0	0	1
TOO AUTOLYZED TO EXAMINE	1	0	0	0
ESOPHAGUS				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1
EYES/OPTIC N.				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
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TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 3

		FEMALE			
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		1	0	0	1
FEMUR					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
GALLBLADDER					
TOTAL NUMBER EXAMINED		0	0	0	0
EXAMINED, UNREMARKABLE		0	0	0	0
TOO AUTOLYZED TO EXAMINE		0	0	0	1
NOT PRESENT FOR EXAMINATION		1	0	0	0
HEART					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
ILEUM					
TOTAL NUMBER EXAMINED		0	0	0	1
EXAMINED, UNREMARKABLE		0	0	0	1
TOO AUTOLYZED TO EXAMINE		1	0	0	0
JEJUNUM					
TOTAL NUMBER EXAMINED		0	0	0	1
EXAMINED, UNREMARKABLE		0	0	0	1
TOO AUTOLYZED TO EXAMINE		1	0	0	0

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

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TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

----- FEMALE -----

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		1	0	0	1
KIDNEYS					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
LAC. GLAND EXOR					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
LARYNX					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
LIVER					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		0	0	0	0
-HYPERTROPHY, HEPATOCELLULAR		0	0	0	1
MODERATE		NONE	NONE	NONE	1
-INFILTRATE, MONONUCLEAR		1	0	0	1
MINIMAL		1	NONE	NONE	1
LUNGS					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		0	0	0	0
-ATELECTASIS		0	0	0	1
MINIMAL		NONE	NONE	NONE	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

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TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

----- FEMALE -----

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		1	0	0	1
LUNGS	- CONTINUED				
-CONGESTION		1	0	0	1
MINIMAL		NONE	NONE	NONE	1
MILD		1	NONE	NONE	NONE
LYMPH NODE, MAND					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
LYMPH NODE, MES					
TOTAL NUMBER EXAMINED		0	0	0	1
EXAMINED, UNREMARKABLE		0	0	0	1
NOT PRESENT FOR EXAMINATION		1	0	0	0
MAMMARY GLAND					
TOTAL NUMBER EXAMINED		0	0	0	0
EXAMINED, UNREMARKABLE		0	0	0	0
NOT PRESENT FOR EXAMINATION		1	0	0	1
MARROW, FEMUR					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		0	0	0	1
-DEPLETION		1	0	0	0
MILD		1	NONE	NONE	NONE

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 6

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	1	0	0	1
MARROW, STERN				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	0	0	0	1
-DEPLETION	1	0	0	0
MILD	1	NONE	NONE	NONE
NASAL LEVEL I				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1
NASAL LEVEL III				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1
NERVE, SCIATIC				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1
OVARIES				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	0	0	0	1
-DECREASED CORPORA LUTEA	1	0	0	0
PRESENT	1	NONE	NONE	NONE

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 7

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		1	0	0	1
OVIDUCTS					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
PANCREAS					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
PARATHYROIDS					
TOTAL NUMBER EXAMINED		0	0	0	0
EXAMINED, UNREMARKABLE		1	0	0	1
NOT PRESENT FOR EXAMINATION		0	0	0	0
PEYER'S PATCHES					
TOTAL NUMBER EXAMINED		0	0	0	1
EXAMINED, UNREMARKABLE		0	0	0	1
TOO AUTOLYZED TO EXAMINE		1	0	0	0
PHARYNX					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
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TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 8

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		1	0	0	1
PITUITARY					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
RECTUM					
TOTAL NUMBER EXAMINED		0	0	0	1
EXAMINED, UNREMARKABLE		0	0	0	1
TOO AUTOLYZED TO EXAMINE		1	0	0	0
SAL. GLAND MAND					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
SKELETAL MUSCLE					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
SKIN					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1
SPINAL CORD					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	0	0	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
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TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 9

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	1	0	0	1
SPLEEN				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	0	0	0	1
-DEPLETION, LYMPHOID	1	0	0	0
MILD	1	NONE	NONE	NONE
STERNUM				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1
STOMACH, GLAN				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	0	0	0	1
-INFILTRATE, NEUTROPHIL	1	0	0	0
MILD	1	NONE	NONE	NONE
-ULCERATION	1	0	0	0
PRESENT	1	NONE	NONE	NONE
STOMACH, NON				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 10

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	1	0	0	1
THYMUS				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	0	0	0	0
-DEPLETION, LYMPHOID	1	0	0	1
MINIMAL	NONE	NONE	NONE	1
MODERATE	1	NONE	NONE	NONE
THYROID GLANDS				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1
TONGUE				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1
TRACHEA				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1
URINARY BLADDER				
TOTAL NUMBER EXAMINED	0	0	0	1
EXAMINED, UNREMARKABLE	0	0	0	1
TOO AUTOLYZED TO EXAMINE	1	0	0	0

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 42 (UNSCHEDULED DEATHS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 11

----- FEMALE -----				
	GROUP: 1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	1	0	0	1
UTERUS				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	1	0	0	1
VAGINA				
TOTAL NUMBER EXAMINED	1	0	0	1
EXAMINED, UNREMARKABLE	0	0	0	0
-ESTROUS CYCLE: DIESTRUS				
PRESENT	1	0	0	1
-LUMINAL DEBRIS, CELLULAR				
MILD	1	0	0	1
1 - 0 MG/KG/DAY 2 - 0.1 MG/KG/DAY 3 - 3 MG/KG/DAY 4 - 30 MG/KG/DAY				

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
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TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 1

MALE				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
ADRENAL CORTEX				
TOTAL NUMBER EXAMINED	10	10	10	10
EXAMINED, UNREMARKABLE	9	10	9	2
- ACCESSORY CORTICAL TISSUE				
PRESENT	1	0	1	2
- HYPERSTROPHY				
MINIMAL	1	NA	1	2
NONE	0	0	0	8
ADRENAL GLANDS				
TOTAL NUMBER EXAMINED	NA	1	NA	NA
EXAMINED, UNREMARKABLE	NA	1	NA	NA
ADRENAL MEDULLA				
TOTAL NUMBER EXAMINED	10	10	10	10
EXAMINED, UNREMARKABLE	10	10	10	10
AORTA				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
BRAIN				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 2

	MALE			
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
CECUM				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
COLON				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
DUODENUM				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
EPIDIDYMIDES				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
ESOPHAGUS				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	9	NA	NA	9
-INFLAMMATION, SUBACUTE				
MILD	1	NA	NA	1
MODERATE	NONE	NA	NA	1
	1	NA	NA	NONE

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 3

	MALE			
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
EYES/OPTIC N.				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
FEMUR				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
GALLBLADDER				
TOTAL NUMBER EXAMINED	9	NA	NA	8
EXAMINED, UNREMARKABLE	9	NA	NA	8
NOT PRESENT FOR EXAMINATION	1	NA	NA	2
HEART				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
ILEUM				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
JEJUNUM				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 4

MALE				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
KIDNEYS				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	8	NA	NA	7
-BASOPHILIC TUBULES	1	NA	NA	0
MINIMAL	1	NA	NA	NONE
-DILATATION, TUBULAR	0	NA	NA	1
MILD	NONE	NA	NA	1
-INFILTRATE, MONONUCLEAR	0	NA	NA	2
MINIMAL	NONE	NA	NA	2
-MINERALIZATION	1	NA	NA	0
MINIMAL	1	NA	NA	NONE
LAC. GLAND EXOR				
TOTAL NUMBER EXAMINED	9	NA	NA	10
EXAMINED, UNREMARKABLE	7	NA	NA	20
NOT PRESENT FOR EXAMINATION	1	NA	NA	0
-INFILTRATE, MONONUCLEAR	2	NA	NA	8
MINIMAL	2	NA	NA	7
MILD	NONE	NA	NA	1
LARYNX				
TOTAL NUMBER EXAMINED	9	NA	NA	10
EXAMINED, UNREMARKABLE	9	NA	NA	10
NOT PRESENT FOR EXAMINATION	1	NA	NA	0

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 5

		MALE			
GROUP:		1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		10	10	10	10
LIVER					
TOTAL NUMBER EXAMINED		10	10	10	10
EXAMINED, UNREMARKABLE		3	2	0	0
-FIBROSIS		0	0	0	1
MILD		NONE	NA	NA	1
-HYPERTROPHY, HEPATOCELLULAR		0	0	10	10
MILD		NONE	NA	8	NONE
MODERATE		NONE	NA	2	10
-INCREASED MITOSES		0	0	0	9
MINIMAL		NONE	NA	NA	6
MILD		NONE	NA	NA	1
MODERATE		NONE	NA	NA	2
-INFILTRATE, MONONUCLEAR		7	8	7	5
MINIMAL		7	8	7	5
-NECROSIS, HEPATOCELLULAR		0	0	1	1
MINIMAL		NONE	NA	1	NONE
MILD		NONE	NA	NA	1
-NECROSIS, SINGLE CELL		0	0	4	10
MINIMAL		NONE	NA	4	10
LUNGS					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	9
-ATELECTASIS		0	NA	NA	1
MODERATE		NONE	NA	NA	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 6

	MALE			
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
LYMPH NODE, MAND				
TOTAL NUMBER EXAMINED	9	NA	1	10
EXAMINED, UNREMARKABLE	9	NA	1	9
NOT PRESENT FOR EXAMINATION	1	NA	0	0
-HEMORRHAGE	0	NA	0	1
MINIMAL	NONE	NA	NA	1
LYMPH NODE, MES				
TOTAL NUMBER EXAMINED	9	NA	NA	10
EXAMINED, UNREMARKABLE	9	NA	NA	10
NOT PRESENT FOR EXAMINATION	1	NA	NA	0
MARROW, FEMUR				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
MARROW, STERN				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
NASAL LEVEL I				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 7

	MALE			
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
NASAL LEVEL III				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	9	NA	NA	10
-INFILTRATE, NEUTROPHIL	1	NA	NA	0
MODERATE	1	NA	NA	NONE
-LUMINAL DEBRIS, CELLULAR	1	NA	NA	0
MINIMAL	1	NA	NA	NONE
NERVE, SCIATIC				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
PANCREAS				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	9
-INFLAMMATION, CHRONIC	0	NA	NA	1
MILD	NONE	NA	NA	1
-PIGMENT, HEMOSIDERIN	0	NA	NA	1
MILD	NONE	NA	NA	1
PARATHYROIDS				
TOTAL NUMBER EXAMINED	3	NA	NA	3
EXAMINED, UNREMARKABLE	3	NA	NA	3
NOT PRESENT FOR EXAMINATION	7	NA	NA	7

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 8

	MALE			
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
PEYER'S PATCHES				
TOTAL NUMBER EXAMINED	9	NA	NA	10
EXAMINED, UNREMARKABLE	9	NA	NA	10
NOT PRESENT FOR EXAMINATION	1	NA	NA	0
PHARYNX				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	9	NA	NA	10
-INFLAMMATION, SUBACUTE	1	NA	NA	0
MODERATE	1	NA	NA	NONE
PITUITARY				
TOTAL NUMBER EXAMINED	8	NA	NA	8
EXAMINED, UNREMARKABLE	8	NA	NA	8
NOT PRESENT FOR EXAMINATION	2	NA	NA	2
PROSTATE				
TOTAL NUMBER EXAMINED	9	NA	NA	10
EXAMINED, UNREMARKABLE	9	NA	NA	10
NOT PRESENT FOR EXAMINATION	1	NA	NA	0
RECTUM				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 9

	MALE			
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
SAL. GLAND MAND				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
SEMINAL VESICLES				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
SKELETAL MUSCLE				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	9
-INFLAMMATION, SUBACUTE	0	NA	NA	1
MINIMAL	NONE	NA	NA	1
SKIN				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
SPINAL CORD				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY
NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 10

	MALE			
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
SPLEEN				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
STERNUM				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
STOMACH, GLAN				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	7
-CYST, KERATIN	0	NA	NA	1
PRESENT	NONE	NA	NA	1
-DILATATION, GLANDULAR	0	NA	NA	1
MINIMAL	NONE	NA	NA	1
-HYPERPLASIA, GLANDULAR	0	NA	NA	1
MINIMAL	NONE	NA	NA	1
-HYPERPLASIA, SQUAMOUS	0	NA	NA	1
MINIMAL	NONE	NA	NA	1
STOMACH, NON				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 11

	MALE			
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
TESTES				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
THYMUS				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	9	NA	NA	9
-HEMORRHAGE	1	NA	NA	0
MILD	1	NA	NA	NONE
-INFLAMMATION, SUBACUTE	0	NA	NA	1
MILD	NONE	NA	NA	1
THYROID GLANDS				
TOTAL NUMBER EXAMINED	8	NA	NA	10
EXAMINED, UNREMARKABLE	5	NA	NA	9
NOT PRESENT FOR EXAMINATION	2	NA	NA	0
-ECTOPIC TISSUE	3	NA	NA	1
PRESENT	3	NA	NA	1
TONGUE				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 43 (WEEK 4 PRIMARY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 12

MALE				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
TRACHEA				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
URINARY BLADDER				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY
NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 1

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
ADRENAL CORTEX				
TOTAL NUMBER EXAMINED	10	10	10	10
EXAMINED, UNREMARKABLE	9	10	8	7
- ACCESSORY CORTICAL TISSUE				
PRESENT	0	0	2	0
NONE	NA	NA	2	NONE
- CONGESTION				
MINIMAL	1	0	0	3
MILD	1	NA	NA	2
NONE	NA	NA	NA	1
ADRENAL MEDULLA				
TOTAL NUMBER EXAMINED	10	10	10	10
EXAMINED, UNREMARKABLE	10	10	10	10
AORTA				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	9
- INFLAMMATION, SUBACUTE				
MINIMAL	0	NA	NA	1
NONE	NA	NA	NA	1
BRAIN				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 2

----- FEMALE -----				
	GROUP: 1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
CECUM				
TOTAL NUMBER EXAMINED	10	NA	NA	9
EXAMINED, UNREMARKABLE	10	NA	NA	9
NOT PRESENT FOR EXAMINATION	0	NA	NA	1
CERVIX				
TOTAL NUMBER EXAMINED	10	10	10	10
EXAMINED, UNREMARKABLE	10	10	10	10
COLON				
TOTAL NUMBER EXAMINED	10	NA	NA	9
EXAMINED, UNREMARKABLE	10	NA	NA	9
NOT PRESENT FOR EXAMINATION	0	NA	NA	1
DUODENUM				
TOTAL NUMBER EXAMINED	10	NA	NA	9
EXAMINED, UNREMARKABLE	10	NA	NA	9
NOT PRESENT FOR EXAMINATION	0	NA	NA	1
ESOPHAGUS				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	9	NA	NA	8
-INFLAMMATION, SUBACUTE	1	NA	NA	2
MINIMAL	1	NA	NA	1
MILD	NONE	NA	NA	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 3

----- FEMALE -----				
	GROUP: 1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
EYES/OPTIC N.				
TOTAL NUMBER EXAMINED	10	1	1	10
EXAMINED, UNREMARKABLE	10	1	1	10
FEMUR				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
GALLBLADDER				
TOTAL NUMBER EXAMINED	10	NA	NA	8
EXAMINED, UNREMARKABLE	10	NA	NA	8
NOT PRESENT FOR EXAMINATION	0	NA	NA	2
HEART				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	9	NA	NA	10
-HYPERPLASIA, MESOTHelial MINIMAL	1	NA	NA	0
ILEUM				
TOTAL NUMBER EXAMINED	10	NA	NA	9
EXAMINED, UNREMARKABLE	10	NA	NA	9
NOT PRESENT FOR EXAMINATION	0	NA	NA	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 4

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		10	10	10	10
JEJUNUM					
TOTAL NUMBER EXAMINED		10	NA	NA	9
EXAMINED, UNREMARKABLE		10	NA	NA	9
NOT PRESENT FOR EXAMINATION		0	NA	NA	1
KIDNEYS					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		4	NA	NA	6
-BASOPHILIC TUBULES		4	NA	NA	3
MINIMAL		4	NA	NA	3
-DILATATION, TUBULAR		1	NA	NA	3
MINIMAL		1	NA	NA	3
-FIBROSIS		1	NA	NA	1
MINIMAL		1	NA	NA	1
-INFILTRATE, MONONUCLEAR		2	NA	NA	1
MINIMAL		2	NA	NA	1
-INFILTRATE, NEUTROPHIL		0	NA	NA	1
MINIMAL		NONE	NA	NA	0
-MINERALIZATION		1	NA	NA	0
MINIMAL		1	NA	NA	NONE
LAC. GLAND EXOR					
TOTAL NUMBER EXAMINED		10	NA	NA	9
EXAMINED, UNREMARKABLE		8	NA	NA	9
NOT PRESENT FOR EXAMINATION		0	NA	NA	1
-INFILTRATE, MONONUCLEAR		2	NA	NA	0
MINIMAL		2	NA	NA	NONE

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 5

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		10	10	10	10
LARYNX					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
LIVER					
TOTAL NUMBER EXAMINED		10	10	10	10
EXAMINED, UNREMARKABLE		0	3	0	0
-HYPERTROPHY, HEPATOCELLULAR		0	0	10	10
MINIMAL		NONE	NA	8	NONE
MILD		NONE	NA	2	NONE
MODERATE		NONE	NA	NA	10
-INCREASED MITOSES		0	0	0	5
MINIMAL		NONE	NA	NA	2
MILD		NONE	NA	NA	3
-INFILTRATE, MONONUCLEAR		10	7	6	10
MINIMAL		10	7	6	10
-NECROSIS, HEPATOCELLULAR		0	1	0	0
MINIMAL		NONE	1	NA	NONE
-NECROSIS, SINGLE CELL		0	0	0	4
MINIMAL		NONE	NA	NA	4
LUNGS					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		5	NA	NA	7
-ATELECTASIS		3	NA	NA	3
MINIMAL		1	NA	NA	1
MILD		2	NA	NA	2

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 6

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		10	10	10	10
LUNGS - CONTINUED					
-HISTIOCYTOSIS, ALVEOLAR		1	NA	NA	1
MINIMAL		NONE	NA	NA	1
MILD		1	NA	NA	NONE
-INFILTRATE, MONONUCLEAR		0	NA	NA	1
MINIMAL		NONE	NA	NA	1
-INFLAMMATION, SUBACUTE		1	NA	NA	0
MINIMAL		1	NA	NA	NONE
LYMPH NODE, MAND					
TOTAL NUMBER EXAMINED		10	NA	NA	9
EXAMINED, UNREMARKABLE		7	NA	NA	5
NOT PRESENT FOR EXAMINATION		0	NA	NA	1
-HEMORRHAGE		3	NA	NA	4
MINIMAL		3	NA	NA	3
MILD		NONE	NA	NA	1
LYMPH NODE, MES					
TOTAL NUMBER EXAMINED		10	NA	NA	9
EXAMINED, UNREMARKABLE		9	NA	NA	9
NOT PRESENT FOR EXAMINATION		0	NA	NA	1
-HEMORRHAGE		1	NA	NA	0
MILD		1	NA	NA	NONE

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
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TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 7

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		10	10	10	10
MAMMARY GLAND					
TOTAL NUMBER EXAMINED		5	NA	NA	7
EXAMINED, UNREMARKABLE		5	NA	NA	7
NOT PRESENT FOR EXAMINATION		5	NA	NA	3
MARROW, FEMUR					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
MARROW, STERN					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
NASAL LEVEL I					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
NASAL LEVEL III					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED		9	NA	NA	9
EXAMINED, UNREMARKABLE		9	NA	NA	9
NOT PRESENT FOR EXAMINATION		1	NA	NA	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
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TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 8

----- FEMALE -----				
	GROUP: 1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
OVARIES				
TOTAL NUMBER EXAMINED	10	10	10	10
EXAMINED, UNREMARKABLE	7	10	10	7
-CYST, FOLLICULAR	3	0	0	3
PRESENT	3	NA	NA	3
OVIDUCTS				
TOTAL NUMBER EXAMINED	10	10	10	10
EXAMINED, UNREMARKABLE	10	10	10	10
PANCREAS				
TOTAL NUMBER EXAMINED	10	NA	NA	9
EXAMINED, UNREMARKABLE	10	NA	NA	9
NOT PRESENT FOR EXAMINATION	0	NA	NA	1
PARATHYROIDS				
TOTAL NUMBER EXAMINED	5	NA	NA	3
EXAMINED, UNREMARKABLE	5	NA	NA	3
NOT PRESENT FOR EXAMINATION	5	NA	NA	7
PEYER'S PATCHES				
TOTAL NUMBER EXAMINED	10	NA	NA	8
EXAMINED, UNREMARKABLE	10	NA	NA	8
NOT PRESENT FOR EXAMINATION	0	NA	NA	2

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 9

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		10	10	10	10
PHARYNX					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
PITUITARY					
TOTAL NUMBER EXAMINED		10	NA	NA	8
EXAMINED, UNREMARKABLE		10	NA	NA	8
NOT PRESENT FOR EXAMINATION		0	NA	NA	2
RECTUM					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		9	NA	NA	10
-CYST, KERATIN		1	NA	NA	0
PRESENT		1	NA	NA	NONE
SAL. GLAND MAND					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		9	NA	NA	10
-INFILTRATE, MONONUCLEAR		1	NA	NA	0
MINIMAL		1	NA	NA	NONE
SKELETAL MUSCLE					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 10

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		10	10	10	10
SKIN					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
SPINAL CORD					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
SPLEEN					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
STERNUM					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
STOMACH, GLAN					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		7	NA	NA	9
-DILATATION, GLANDULAR		1	NA	NA	1
MINIMAL		1	NA	NA	1
-HYPERPLASIA, SQUAMOUS		1	NA	NA	0
MINIMAL		1	NA	NA	NONE
-INFILTRATE, NEUTROPHIL		1	NA	NA	0
MILD		1	NA	NA	NONE

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

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TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		10	10	10	10
STOMACH, GLAN - CONTINUED					
STOMACH, NON					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
TAIL					
TOTAL NUMBER EXAMINED		1	NA	1	NA
EXAMINED, UNREMARKABLE		0	NA	0	NA
-EXUDATE, EPIDERMAL SURFACE		0	NA	1	NA
MILD		NA	NA	1	NA
-HEMORRHAGE		0	NA	1	NA
MILD		NA	NA	1	NA
-INFILTRATE, NEUTROPHIL		1	NA	1	NA
MINIMAL		1	NA	NA	NA
MILD		NA	NA	1	NA
THYMUS					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		7	NA	NA	10
-HEMORRHAGE		2	NA	NA	0
MINIMAL		1	NA	NA	NONE
MILD		1	NA	NA	NONE
-INFILTRATE, NEUTROPHIL		1	NA	NA	0
MILD		1	NA	NA	NONE

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 12

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		10	10	10	10
THYMUS	- CONTINUED				
-NECROSIS		1	NA	NA	0
MILD		1	NA	NA	NONE
THYROID GLANDS					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		9	NA	NA	10
-ECTOPIC TISSUE		1	NA	NA	0
PRESENT		1	NA	NA	NONE
TONGUE					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
TRACHEA					
TOTAL NUMBER EXAMINED		10	NA	NA	10
EXAMINED, UNREMARKABLE		10	NA	NA	10
URINARY BLADDER					
TOTAL NUMBER EXAMINED		9	NA	NA	10
EXAMINED, UNREMARKABLE		9	NA	NA	10
NOT PRESENT FOR EXAMINATION		1	NA	NA	0

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 44 (WEEK 4 PRIMARY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 13

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	10	10	10
UTERUS				
TOTAL NUMBER EXAMINED	10	10	10	10
EXAMINED, UNREMARKABLE	8	9	8	10
-DILATATION, LUMEN	2	1	2	0
MINIMAL	2	1	2	NONE
-EDEMA	1	0	0	0
MILD	1	NA	NA	NONE
VAGINA				
TOTAL NUMBER EXAMINED	10	10	10	10
EXAMINED, UNREMARKABLE	0	0	0	0
-ESTROUS CYCLE: DIESTRUS	3	6	5	10
PRESENT	3	6	5	10
-ESTROUS CYCLE: ESTRUS	5	2	2	0
PRESENT	5	2	2	NONE
-ESTROUS CYCLE: PROESTRUS	2	2	3	0
PRESENT	2	2	3	NONE

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 45 (WEEK 8 RECOVERY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 1

MALE				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	0	0	10
ADRENAL CORTEX				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	9
-ACCESSORY CORTICAL TISSUE	0	NA	NA	1
PRESENT	NA	NA	NA	1
ADRENAL MEDULLA				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	10	NA	NA	10
KIDNEYS				
TOTAL NUMBER EXAMINED	NA	NA	NA	1
EXAMINED, UNREMARKABLE	NA	NA	NA	0
-BASOPHILIC TUBULES	NA	NA	NA	1
MINIMAL	NA	NA	NA	1
-INFILTRATE, MONONUCLEAR	NA	NA	NA	1
MINIMAL	NA	NA	NA	1
-NECROSIS, TUBULAR	NA	NA	NA	1
MINIMAL	NA	NA	NA	1
LIVER				
TOTAL NUMBER EXAMINED	10	NA	NA	10
EXAMINED, UNREMARKABLE	4	NA	NA	0
-INFILTRATE, MONONUCLEAR	6	NA	NA	10
MINIMAL	6	NA	NA	9
MILD	NA	NA	NA	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY
NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 45 (WEEK 8 RECOVERY NECROPSY - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 2

MALE				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	10	0	0	10
LIVER - CONTINUED				
-NECROSIS, HEPATOCELLULAR	1	NA	NA	1
MINIMAL	1	NA	NA	1
LYMPH NODE, MAND				
TOTAL NUMBER EXAMINED	1	NA	NA	1
EXAMINED, UNREMARKABLE	0	NA	NA	0
-PLASMACYTOSIS	1	NA	NA	1
MINIMAL	NA	NA	NA	1
MILD	1	NA	NA	NA
TESTES				
TOTAL NUMBER EXAMINED	NA	NA	NA	1
EXAMINED, UNREMARKABLE	NA	NA	NA	0
-NECROSIS	NA	NA	NA	1
SEVERE	NA	NA	NA	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 46 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 1

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	9	0	0	9
ADIPOSE TISSUE				
TOTAL NUMBER EXAMINED	1	NA	NA	NA
EXAMINED, UNREMARKABLE	0	NA	NA	NA
-BACTERIAL COLONIES	1	NA	NA	NA
PRESENT	1	NA	NA	NA
-FOREIGN MATERIAL	1	NA	NA	NA
PRESENT	1	NA	NA	NA
-INFLAMMATION, PYOGRANULOMATOUS	1	NA	NA	NA
MODERATE	1	NA	NA	NA
ADRENAL CORTEX				
TOTAL NUMBER EXAMINED	9	NA	NA	9
EXAMINED, UNREMARKABLE	7	NA	NA	7
-ACCESSORY CORTICAL TISSUE	2	NA	NA	2
PRESENT	2	NA	NA	2
ADRENAL MEDULLA				
TOTAL NUMBER EXAMINED	9	NA	NA	9
EXAMINED, UNREMARKABLE	9	NA	NA	9
CERVIX				
TOTAL NUMBER EXAMINED	9	NA	NA	9
EXAMINED, UNREMARKABLE	9	NA	NA	9

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 46 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 2

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	9	0	0	9
ESOPHAGUS				
TOTAL NUMBER EXAMINED	NA	NA	NA	1
EXAMINED, UNREMARKABLE	NA	NA	NA	0
-FOREIGN MATERIAL	NA	NA	NA	1
PRESENT	NA	NA	NA	1
-INFLAMMATION, PYOGRANULOMATOUS	NA	NA	NA	1
MODERATE	NA	NA	NA	1
LIVER				
TOTAL NUMBER EXAMINED	9	NA	NA	9
EXAMINED, UNREMARKABLE	2	NA	NA	2
-INFILTRATE, MONONUCLEAR	7	NA	NA	7
MINIMAL	6	NA	NA	6
MILD	1	NA	NA	1
-NECROSIS, HEPATOCELLULAR	0	NA	NA	2
MINIMAL	NA	NA	NA	2
LYMPH NODE, BRON				
TOTAL NUMBER EXAMINED	1	NA	NA	1
EXAMINED, UNREMARKABLE	0	NA	NA	0
-FOREIGN MATERIAL	1	NA	NA	0
PRESENT	1	NA	NA	NA
-INFLAMMATION, PYOGRANULOMATOUS	1	NA	NA	0
MODERATE	1	NA	NA	NA

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 46 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 3

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	9	0	0	9
LYMPH NODE, BRON - CONTINUED				
-PLASMACYTOSIS	0	NA	NA	1
MINIMAL	NA	NA	NA	1
LYMPH NODE, MAND				
TOTAL NUMBER EXAMINED	1	NA	NA	1
EXAMINED, UNREMARKABLE	0	NA	NA	0
-PLASMACYTOSIS	1	NA	NA	1
MILD	1	NA	NA	NA
MODERATE	NA	NA	NA	1
LYMPH NODE, MED				
TOTAL NUMBER EXAMINED	1	NA	NA	1
EXAMINED, UNREMARKABLE	0	NA	NA	0
-PLASMACYTOSIS	1	NA	NA	1
MILD	1	NA	NA	1
MAMMARY GLAND				
TOTAL NUMBER EXAMINED	NA	NA	NA	1
EXAMINED, UNREMARKABLE	NA	NA	NA	0
-FOREIGN MATERIAL	NA	NA	NA	1
PRESENT	NA	NA	NA	1
-INFLAMMATION, PYOGRANULOMATOUS	NA	NA	NA	1
MODERATE	NA	NA	NA	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 46 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 4

----- FEMALE -----					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		20	10	10	20
NUMBER OF ANIMALS EXAMINED		9	0	0	9
OVARIES					
TOTAL NUMBER EXAMINED		9	NA	NA	9
EXAMINED, UNREMARKABLE		9	NA	NA	8
-CYST, FOLLICULAR		0	NA	NA	1
PRESENT		NA	NA	NA	1
OVIDUCTS					
TOTAL NUMBER EXAMINED		9	NA	NA	9
EXAMINED, UNREMARKABLE		9	NA	NA	9
SKIN					
TOTAL NUMBER EXAMINED		NA	NA	NA	1
EXAMINED, UNREMARKABLE		NA	NA	NA	0
-FOREIGN MATERIAL		NA	NA	NA	1
PRESENT		NA	NA	NA	1
-INFLAMMATION, PYOGRANULOMATOUS		NA	NA	NA	1
MODERATE		NA	NA	NA	1
SPLEEN					
TOTAL NUMBER EXAMINED		NA	NA	NA	1
EXAMINED, UNREMARKABLE		NA	NA	NA	0
-HEMATOPOIESIS, EXTRAMEDULLARY		NA	NA	NA	1
MILD		NA	NA	NA	1

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY
NA = NOT APPLICABLE

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE 46 (WEEK 8 RECOVERY NECROPSY - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
SUMMARY OF MICROSCOPIC FINDINGS

PAGE 5

----- FEMALE -----				
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	20	10	10	20
NUMBER OF ANIMALS EXAMINED	9	0	0	9
UTERUS				
TOTAL NUMBER EXAMINED	9	NA	NA	9
EXAMINED, UNREMARKABLE	8	NA	NA	8
-DILATATION, LUMEN	1	NA	NA	1
MINIMAL	1	NA	NA	1
VAGINA				
TOTAL NUMBER EXAMINED	9	NA	NA	8
EXAMINED, UNREMARKABLE	0	NA	NA	0
NOT PRESENT FOR EXAMINATION	0	NA	NA	1
-ESTROUS CYCLE: DIESTRUS				
PRESENT	7	NA	NA	7
-ESTROUS CYCLE: ESTRUS				
PRESENT	2	NA	NA	0
-ESTROUS CYCLE: PROESTRUS				
PRESENT	0	NA	NA	1
NA = NOT APPLICABLE				

1- 0 MG/KG/DAY 2- 0.1 MG/KG/DAY 3- 3 MG/KG/DAY 4- 30 MG/KG/DAY

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APPENDIX A

Individual Animal Data

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
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SPONSOR NO.: DUPONT-24459

TABLE A1 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL SURVIVAL AND DISPOSITION

PAGE 1

ANIMAL	SEX	GROUP	TYPE OF DEATH	AGE IN WEEKS A	DATE OF DEATH	DAYS ON STUDY
90903	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90905	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90911	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90912	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90915	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90917	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90922	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90925	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90929	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90932	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90939	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90940	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90942	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90943	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90945	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90953	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90958	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90959	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90961	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90965	M	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90908	M	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90914	M	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90924	M	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90934	M	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90938	M	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90946	M	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90951	M	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90954	M	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90956	M	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28

A = CALCULATED TO THE NEAREST WHOLE WEEK USING THE MEAN AGE IN WEEKS AT INITIATION OF DOSING (7)

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TABLE A1 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL SURVIVAL AND DISPOSITION

PAGE 2

ANIMAL	SEX	GROUP	TYPE OF DEATH	AGE IN WEEKS A	DATE OF DEATH	DAYS ON STUDY
90963	M	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90907	M	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90913	M	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90919	M	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90927	M	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90948	M	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90949	M	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90960	M	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90966	M	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90967	M	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90969	M	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90902	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90904	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90906	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90910	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90920	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90923	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90926	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90930	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90931	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90935	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90937	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90941	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90944	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90947	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90950	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90952	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90955	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28

A = CALCULATED TO THE NEAREST WHOLE WEEK USING THE MEAN AGE IN WEEKS AT INITIATION OF DOSING (7)

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A1 (MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL SURVIVAL AND DISPOSITION

PAGE 3

ANIMAL	SEX	GROUP	TYPE OF DEATH	AGE IN WEEKS A	DATE OF DEATH	DAYS ON STUDY
90962	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	15-JAN-08	28
90964	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58
90968	M	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	58

A = CALCULATED TO THE NEAREST WHOLE WEEK USING THE MEAN AGE IN WEEKS AT INITIATION OF DOSING (7)

PDEADv4.05
04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A2 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL SURVIVAL AND DISPOSITION

PAGE 1

ANIMAL	SEX	GROUP	TYPE OF DEATH	AGE IN WEEKS A	DATE OF DEATH	DAYS ON STUDY
90975	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
90984	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
90985	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
90986	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90992	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90995	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90997	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90999	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91000	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91002	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91015	F	0 MG/KG/DAY	FOUND DEAD	10	13-JAN-08	25
91016	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91018	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91019	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91021	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91024	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91025	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91028	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91030	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91037	F	0 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90977	F	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90981	F	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90996	F	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90998	F	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91011	F	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91020	F	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91031	F	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91033	F	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91035	F	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28

A = CALCULATED TO THE NEAREST WHOLE WEEK USING THE MEAN AGE IN WEEKS AT INITIATION OF DOSING (7)

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A2 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL SURVIVAL AND DISPOSITION

PAGE 2

ANIMAL	SEX	GROUP	TYPE OF DEATH	AGE IN WEEKS A	DATE OF DEATH	DAYS ON STUDY
91038	F	0.1 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90973	F	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90988	F	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90990	F	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90993	F	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91006	F	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91013	F	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91017	F	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91023	F	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91032	F	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91034	F	3 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90972	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
90976	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90978	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90983	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
90987	F	30 MG/KG/DAY	FOUND DEAD	8	28-DEC-07	9
90991	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91001	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91003	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91004	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91005	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91007	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91008	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91010	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91012	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91014	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91026	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91027	F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28

A = CALCULATED TO THE NEAREST WHOLE WEEK USING THE MEAN AGE IN WEEKS AT INITIATION OF DOSING (7)

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A2 (FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL SURVIVAL AND DISPOSITION

PAGE 3

ANIMAL SEX	GROUP	TYPE OF DEATH	AGE IN WEEKS A	DATE OF DEATH	DAYS ON STUDY
91029 F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	15	14-FEB-08	57
91039 F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28
91040 F	30 MG/KG/DAY	SCHEDULED EUTHANASIA	11	16-JAN-08	28

A = CALCULATED TO THE NEAREST WHOLE WEEK USING THE MEAN AGE IN WEEKS AT INITIATION OF DOSING (7)

PDEADv4.05
04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 1

STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90903	M	0 MG/KG/DAY	NORMAL	0	7:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	7:02	P	RECOVERY NECROPSY (WEEK 8)
90905	M	0 MG/KG/DAY	DISPOSITION	0	7:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	7:02	P	RECOVERY NECROPSY (WEEK 8)
90911	M	0 MG/KG/DAY	DISPOSITION	0	7:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	7:02	P	RECOVERY NECROPSY (WEEK 8)

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
210

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 2

STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90911	M	0 MG/KG/DAY	BODY/INTEG III	35	8:36	P	WET YELLOW MATERIAL UROGENITAL AREA
90912	M	0 MG/KG/DAY	NORMAL	0	7:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90912	M	0 MG/KG/DAY	DISPOSITION	58	7:02	P	RECOVERY NECROPSY (WEEK 8)
90912	M	0 MG/KG/DAY	EYES/EARS/NOSE	28	7:14	P	ABNORMAL PUPIL POSITION LEFT EYE
				35	8:38	P	ABNORMAL PUPIL POSITION LEFT EYE
				42	7:35	P	ABNORMAL PUPIL POSITION LEFT EYE
				49	8:54	P	ABNORMAL PUPIL POSITION LEFT EYE
				58	6:18	P	ABNORMAL PUPIL POSITION LEFT EYE
90915	M	0 MG/KG/DAY	NORMAL	0	7:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90915	M	0 MG/KG/DAY	DISPOSITION	28	9:25	P	PRIMARY NECROPSY (DAY 28)
90917	M	0 MG/KG/DAY	NORMAL	0	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90917	M	0 MG/KG/DAY	DISPOSITION	58	7:02	P	RECOVERY NECROPSY (WEEK 8)
90922	M	0 MG/KG/DAY	NORMAL	0	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 3

STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90922	M	0 MG/KG/DAY	NORMAL	14	8:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90922	M	0 MG/KG/DAY	DISPOSITION	58	7:02	P	RECOVERY NECROPSY (WEEK 8)
90925	M	0 MG/KG/DAY		0	8:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90925	M	0 MG/KG/DAY		28	9:25	P	PRIMARY NECROPSY (DAY 28)
90929	M	0 MG/KG/DAY	NORMAL	0	8:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90929	M	0 MG/KG/DAY		28	9:26	P	PRIMARY NECROPSY (DAY 28)
90932	M	0 MG/KG/DAY		0	8:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
			DISPOSITION	7	6:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 4

STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90932	M	0 MG/KG/DAY	DISPOSITION	58	7:02	P	RECOVERY NECROPSY (WEEK 8)
90939	M	0 MG/KG/DAY	NORMAL	0	8:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90939	M	0 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90940	M	0 MG/KG/DAY	NORMAL	0	8:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90940	M	0 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90940	M	0 MG/KG/DAY	BODY/INTEG II	14	8:55	P	SCABBING MEDIAL TAIL
90942	M	0 MG/KG/DAY	NORMAL	0	8:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90942	M	0 MG/KG/DAY	DISPOSITION	58	7:02	P	RECOVERY NECROPSY (WEEK 8)
90943	M	0 MG/KG/DAY	NORMAL	0	8:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90943	M	0 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 5

STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE OBSERVATIONS	
						GRADE	OBSERVATIONS
90945	M	0 MG/KG/DAY	NORMAL	0	8:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	7:02	P	RECOVERY NECROPSY (WEEK 8)
90953	M	0 MG/KG/DAY	DISPOSITION NORMAL	0	8:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90953	M	0 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
				0	8:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90958	M	0 MG/KG/DAY	DISPOSITION	28	7:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				0	8:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90958	M	0 MG/KG/DAY	DISPOSITION	28	7:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				0	8:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90959	M	0 MG/KG/DAY	DISPOSITION	58	7:03	P	RECOVERY NECROPSY (WEEK 8)
				0	8:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90959	M	0 MG/KG/DAY	NORMAL	21	11:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90959	M	0 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90961	M	0 MG/KG/DAY	NORMAL	0	8:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90961	M	0 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90965	M	0 MG/KG/DAY	NORMAL	0	8:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90965	M	0 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90908	M	0.1 MG/KG/DAY	NORMAL	0	8:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90908	M	0.1 MG/KG/DAY	DISPOSITION	28	9:25	P	PRIMARY NECROPSY (DAY 28)
90914	M	0.1 MG/KG/DAY	NORMAL	0	8:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90914	M	0.1 MG/KG/DAY	DISPOSITION	28	9:25	P	PRIMARY NECROPSY (DAY 28)
90924	M	0.1 MG/KG/DAY	NORMAL	0	8:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS	
90924	M	0.1 MG/KG/DAY	NORMAL	14	9:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	11:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	7:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
90924	M	0.1 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)	
90934	M	0.1 MG/KG/DAY	NORMAL	14	9:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
90934	M	0.1 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)	
90934	M	0.1 MG/KG/DAY	EYES/EARS/NOSE	0	8:22	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				7	6:30	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				21	11:42	P	ABNORMAL PUPIL POSITION LEFT EYE	
				28	7:24	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				0	8:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
90938	M	0.1 MG/KG/DAY	NORMAL	7	6:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	11:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	9:26	P	PRIMARY NECROPSY (DAY 28)	
90946	M	0.1 MG/KG/DAY	DISPOSITION	0	8:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	6:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	11:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	7:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
90946	M	0.1 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)	
				0	8:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	11:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	7:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
90951	M	0.1 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)	
90951	M	0.1 MG/KG/DAY	EYES/EARS/NOSE	7	6:31	P	OPACITY RIGHT EYE	
90954	M	0.1 MG/KG/DAY	NORMAL	0	8:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90954	M	0.1 MG/KG/DAY	NORMAL	7	6:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90954	M	0.1 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90956	M	0.1 MG/KG/DAY		0	8:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
			NORMAL	21	11:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90956	M	0.1 MG/KG/DAY		28	9:26	P	PRIMARY NECROPSY (DAY 28)
90963	M	0.1 MG/KG/DAY		0	8:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
			DISPOSITION	7	6:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	11:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90963	M	0.1 MG/KG/DAY	DISPOSITION	28	9:27	P	PRIMARY NECROPSY (DAY 28)
90907	M	3 MG/KG/DAY		14	9:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90907	M	3 MG/KG/DAY		28	9:25	P	PRIMARY NECROPSY (DAY 28)
90907	M	3 MG/KG/DAY	EYES/EARS/NOSE	0	8:31	P	ABNORMAL PUPIL POSITION RIGHT EYE
				7	6:32	P	ABNORMAL PUPIL POSITION RIGHT EYE
				21	12:00	P	ABNORMAL PUPIL POSITION LEFT EYE
				28	7:29	P	ABNORMAL PUPIL POSITION RIGHT EYE
90913	M	3 MG/KG/DAY	NORMAL	0	8:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
			DISPOSITION	28	7:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90913	M	3 MG/KG/DAY		28	9:25	P	PRIMARY NECROPSY (DAY 28)

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90919	M	3 MG/KG/DAY	NORMAL	0	8:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90919	M	3 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90927	M	3 MG/KG/DAY		0	8:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
			NORMAL	28	7:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90927	M	3 MG/KG/DAY		28	9:26	P	PRIMARY NECROPSY (DAY 28)
90948	M	3 MG/KG/DAY		0	8:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
			DISPOSITION	21	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90948	M	3 MG/KG/DAY		28	9:26	P	PRIMARY NECROPSY (DAY 28)
90949	M	3 MG/KG/DAY		0	8:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
			NORMAL	14	9:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90949	M	3 MG/KG/DAY		28	9:26	P	PRIMARY NECROPSY (DAY 28)
90960	M	3 MG/KG/DAY	DISPOSITION	14	9:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90960	M	3 MG/KG/DAY		28	9:26	P	PRIMARY NECROPSY (DAY 28)
90960	M	3 MG/KG/DAY		0	8:38	P	ABNORMAL PUPIL POSITION LEFT EYE
			EYES/EARS/NOSE	7	6:35	P	ABNORMAL PUPIL POSITION LEFT EYE
				21	12:09	P	ABNORMAL PUPIL POSITION LEFT EYE

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90960	M	3 MG/KG/DAY	EYES/EARS/NOSE	28	7:32	P	ABNORMAL PUPIL POSITION LEFT EYE
90966	M	3 MG/KG/DAY	NORMAL	0	8:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90966	M	3 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90967	M	3 MG/KG/DAY	NORMAL	0	8:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90967	M	3 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90969	M	3 MG/KG/DAY	NORMAL	0	8:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90969	M	3 MG/KG/DAY	DISPOSITION	28	9:27	P	PRIMARY NECROPSY (DAY 28)
90902	M	30 MG/KG/DAY	NORMAL	0	8:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90902	M	30 MG/KG/DAY	DISPOSITION	28	9:25	P	PRIMARY NECROPSY (DAY 28)
90904	M	30 MG/KG/DAY	NORMAL	0	8:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE OBSERVATIONS	
90904	M	30 MG/KG/DAY	NORMAL	28	7:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90904	M	30 MG/KG/DAY	DISPOSITION	28	9:25	P	PRIMARY NECROPSY (DAY 28)
90906	M	30 MG/KG/DAY	NORMAL	0	8:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90906	M	30 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90910	M	30 MG/KG/DAY	NORMAL	0	8:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	9:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90910	M	30 MG/KG/DAY	DISPOSITION	58	7:03	P	RECOVERY NECROPSY (WEEK 8)
90920	M	30 MG/KG/DAY	NORMAL	14	9:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90920	M	30 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90920	M	30 MG/KG/DAY	EYES/EARS/NOSE	0	8:48	P	ABNORMAL PUPIL POSITION LEFT EYE
				7	6:37	P	ABNORMAL PUPIL POSITION LEFT EYE
				21	12:15	P	ABNORMAL PUPIL POSITION LEFT EYE
90923	M	30 MG/KG/DAY	NORMAL	0	8:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90923	M	30 MG/KG/DAY	NORMAL	35	8:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	9:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90923	M	30 MG/KG/DAY	DISPOSITION	58	7:03	P	RECOVERY NECROPSY (WEEK 8)
				0	8:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90926	M	30 MG/KG/DAY	NORMAL	7	6:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90926	M	30 MG/KG/DAY	DISPOSITION	21	12:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90930	M	30 MG/KG/DAY	NORMAL	28	9:26	P	PRIMARY NECROPSY (DAY 28)
				0	8:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90930	M	30 MG/KG/DAY	DISPOSITION	7	6:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90930	M	30 MG/KG/DAY	DISPOSITION	21	12:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90931	M	30 MG/KG/DAY	NORMAL	35	8:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90931	M	30 MG/KG/DAY	DISPOSITION	49	9:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90931	M	30 MG/KG/DAY	DISPOSITION	58	7:03	P	RECOVERY NECROPSY (WEEK 8)
				0	8:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90931	M	30 MG/KG/DAY	ORAL/DENTAL	7	6:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90931	M	30 MG/KG/DAY	DISPOSITION	28	7:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:20	P	WET RED MATERIAL AROUND MOUTH
90935	M	30 MG/KG/DAY	NORMAL	0	8:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90935	M	30 MG/KG/DAY	NORMAL	14	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	9:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90935	M	30 MG/KG/DAY	DISPOSITION	58	7:03	P	RECOVERY NECROPSY (WEEK 8)
90935	M	30 MG/KG/DAY	SPECIAL II	58	6:24	P	TAIL BROKEN
90937	M	30 MG/KG/DAY	NORMAL	0	8:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	9:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90937	M	30 MG/KG/DAY	DISPOSITION	58	7:03	P	RECOVERY NECROPSY (WEEK 8)
90941	M	30 MG/KG/DAY	NORMAL	0	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	9:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90941	M	30 MG/KG/DAY	DISPOSITION	58	7:03	P	RECOVERY NECROPSY (WEEK 8)
90944	M	30 MG/KG/DAY	NORMAL	0	8:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 14

STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME			GRADE	OBSERVATIONS
90944	M	30 MG/KG/DAY	NORMAL	7	6:40	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				14	9:30	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				21	12:24	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				28	7:40	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				35	8:55	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				42	7:47	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				49	9:07	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				58	6:26	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				58	7:03	P	RECOVERY NECROPSY (WEEK 8)		
				90947	M	30 MG/KG/DAY	DISPOSITION		
90947	M	30 MG/KG/DAY	NORMAL	0	8:59	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				7	6:41	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				14	9:30	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				21	12:25	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				28	7:40	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				35	8:56	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				42	7:49	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				49	9:08	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				58	6:26	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				58	7:03	P	RECOVERY NECROPSY (WEEK 8)		
90950	M	30 MG/KG/DAY	DISPOSITION	0	9:00	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				7	6:41	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				14	9:31	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				21	12:26	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				28	7:41	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				90950	M	30 MG/KG/DAY	DISPOSITION		
				28	9:26	P	PRIMARY NECROPSY (DAY 28)		
				90952	M	30 MG/KG/DAY	NORMAL		
				14	9:32	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS	
				90952	M	30 MG/KG/DAY	DISPOSITION		
				28	9:26	P	PRIMARY NECROPSY (DAY 28)		
				90952	M	30 MG/KG/DAY	EYES/EARS/NOSE		
				0	9:01	P	ABNORMAL PUPIL POSITION	LEFT EYE	
				0	9:01	P	ABNORMAL PUPIL POSITION	RIGHT EYE	

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 15

STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90952	M	30 MG/KG/DAY	EYES/EARS/NOSE	7	6:41	P	ABNORMAL PUPIL POSITION RIGHT EYE
				21	12:27	P	ABNORMAL PUPIL POSITION LEFT EYE
				21	12:27	P	ABNORMAL PUPIL POSITION RIGHT EYE
				28	7:42	P	ABNORMAL PUPIL POSITION RIGHT EYE
90955	M	30 MG/KG/DAY	NORMAL	0	9:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90955	M	30 MG/KG/DAY	DISPOSITION	28	9:26	P	PRIMARY NECROPSY (DAY 28)
90962	M	30 MG/KG/DAY		0	9:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90962	M	30 MG/KG/DAY	NORMAL	7	6:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	9:27	P	PRIMARY NECROPSY (DAY 28)
90964	M	30 MG/KG/DAY	DISPOSITION	0	9:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	6:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	9:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90964	M	30 MG/KG/DAY	DISPOSITION	58	6:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	7:03	P	RECOVERY NECROPSY (WEEK 8)
				7	6:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90968	M	30 MG/KG/DAY	NORMAL	21	12:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A3 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 58

ANIMAL	SEX	GROUP	CATEGORY	STUDY	TIME	GRADE	OBSERVATIONS
				DAY			
90968	M	30 MG/KG/DAY	NORMAL	28	7:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	8:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	7:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	9:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	6:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				58	7:03	P	RECOVERY NECROPSY (WEEK 8)
90968	M	30 MG/KG/DAY	DISPOSITION	58			
90968	M	30 MG/KG/DAY	EYES/EARS/NOSE	0	9:06	P	ABNORMAL PUPIL POSITION LEFT EYE

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PCRDv4.11
04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 1

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE OBSERVATIONS		
						DISPOSITION	CLINICAL OBSERVATIONS	
90975	F	0 MG/KG/DAY	NORMAL	0	8:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	9:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	9:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				35	7:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				42	8:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				49	8:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	6:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	7:04	P	RECOVERY NECROPSY (WEEK 8)	
			DISPOSITION	57	7:22	P	SCABBING RIGHT EAR	
90975	F	0 MG/KG/DAY		28	9:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	7:04	P	RECOVERY NECROPSY (WEEK 8)	
				0	8:32	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				7	9:25	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				14	9:26	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				28	7:23	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				35	7:52	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				42	8:22	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				49	8:07	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				57	6:30	P	ABNORMAL PUPIL POSITION RIGHT EYE	
90984	F	0 MG/KG/DAY	NORMAL	0	8:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	9:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	9:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				35	7:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				42	8:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				49	8:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	6:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	7:04	P	RECOVERY NECROPSY (WEEK 8)	
GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT								

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 2

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90985	F	0 MG/KG/DAY	BODY/INTEG II	28	7:24	P	SCABBING RIGHT EAR
90986	F	0 MG/KG/DAY	NORMAL	0	8:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90986	F	0 MG/KG/DAY	DISPOSITION	28	8:45	P	PRIMARY NECROPSY (DAY 28)
90992	F	0 MG/KG/DAY	NORMAL	0	8:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90992	F	0 MG/KG/DAY	DISPOSITION	28	8:45	P	PRIMARY NECROPSY (DAY 28)
90995	F	0 MG/KG/DAY	NORMAL	0	8:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90995	F	0 MG/KG/DAY	DISPOSITION	28	8:45	P	PRIMARY NECROPSY (DAY 28)
90997	F	0 MG/KG/DAY	NORMAL	0	8:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90997	F	0 MG/KG/DAY	DISPOSITION	28	8:45	P	PRIMARY NECROPSY (DAY 28)
90999	F	0 MG/KG/DAY	NORMAL	0	8:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 3

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS	
90999	F	0 MG/KG/DAY	NORMAL	28	7:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				35	7:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				42	8:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				49	8:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	6:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
90999	F	0 MG/KG/DAY	DISPOSITION	57	7:04	P	RECOVERY NECROPSY (WEEK 8)	
91000	F	0 MG/KG/DAY		0	8:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	9:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	9:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	7:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
91000	F	0 MG/KG/DAY	DISPOSITION	28	8:45	P	PRIMARY NECROPSY (DAY 28)	
91002	F	0 MG/KG/DAY		0	8:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	9:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	9:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	7:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
91002	F	0 MG/KG/DAY	DISPOSITION	28	8:45	P	PRIMARY NECROPSY (DAY 28)	
91015	F	0 MG/KG/DAY		0	8:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	9:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				25	6:38	P	FOUND DEAD	
				21	9:21	P	DERMAL ATONIA	
91015	F	0 MG/KG/DAY	BODY/INTEGUMENT	21	9:21	P	THIN	
				21	9:21	P	WET RED MATERIAL AROUND NOSE	
				21	9:21	P	DEFECATION DECREASED	
91015	F	0 MG/KG/DAY	EYES/EARS/NOSE	21	9:21	P	FECES SMALLER THAN NORMAL	
				21	9:21	P	EXCRETA	
				0	8:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
91016	F	0 MG/KG/DAY	NORMAL	7	9:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 4

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
91016	F	0 MG/KG/DAY	NORMAL	14	9:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91016	F	0 MG/KG/DAY	DISPOSITION	28	8:45	P	PRIMARY NECROPSY (DAY 28)
91016	F	0 MG/KG/DAY	BODY/INTEG II	21	9:23	P	SCABBING END OF TAIL
91018	F	0 MG/KG/DAY	NORMAL	0	8:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91018	F	0 MG/KG/DAY	DISPOSITION	28	8:45	P	PRIMARY NECROPSY (DAY 28)
91019	F	0 MG/KG/DAY	NORMAL	0	8:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91019	F	0 MG/KG/DAY	DISPOSITION	28	8:45	P	PRIMARY NECROPSY (DAY 28)
91021	F	0 MG/KG/DAY	NORMAL	0	8:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	7:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	8:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91021	F	0 MG/KG/DAY	DISPOSITION	57	7:04	P	RECOVERY NECROPSY (WEEK 8)
91021	F	0 MG/KG/DAY	ORAL/DENTAL	28	7:34	P	UPPER INCISOR(S) MISSING
91021	F	0 MG/KG/DAY	SPECIAL II	57	6:32	P	TAIL BROKEN
91024	F	0 MG/KG/DAY	NORMAL	0	8:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 5

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE OBSERVATIONS	
						DISPOSITION	
91024	F	0 MG/KG/DAY	NORMAL	21	9:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	7:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	8:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	6:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	7:04	P	RECOVERY NECROPSY (WEEK 8)
			DISPOSITION	21	9:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	8:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91025	F	0 MG/KG/DAY	EYES/EARS/NOSE	57	7:04	P	RECOVERY NECROPSY (WEEK 8)
				0	8:41	P	ABNORMAL PUPIL POSITION RIGHT EYE
				7	9:33	P	ABNORMAL PUPIL POSITION RIGHT EYE
				14	9:30	P	ABNORMAL PUPIL POSITION RIGHT EYE
				35	7:55	P	ABNORMAL PUPIL POSITION RIGHT EYE
				57	6:33	P	ABNORMAL PUPIL POSITION RIGHT EYE
91028	F	0 MG/KG/DAY	NORMAL	0	8:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	7:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	8:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	6:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	7:04	P	RECOVERY NECROPSY (WEEK 8)
91030	F	0 MG/KG/DAY	DISPOSITION	21	9:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	8:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 6

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS	
91030	F	0 MG/KG/DAY	NORMAL	49	8:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
91030	F	0 MG/KG/DAY	DISPOSITION	57	7:04	P	RECOVERY NECROPSY (WEEK 8)	
91030	F	0 MG/KG/DAY	EYES/EARS/NOSE	0	8:42	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				7	9:34	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				14	9:31	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				28	7:38	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				35	7:56	P	ABNORMAL PUPIL POSITION RIGHT EYE	
				57	6:34	P	ABNORMAL PUPIL POSITION RIGHT EYE	
91037	F	0 MG/KG/DAY	NORMAL	0	8:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	9:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	7:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
91037	F	0 MG/KG/DAY	DISPOSITION	28	8:45	P	PRIMARY NECROPSY (DAY 28)	
91037	F	0 MG/KG/DAY	SPECIAL II	21	9:29	P	DIGIT(S) MISSING LEFT FORELIMB	
90977	F	0.1 MG/KG/DAY	NORMAL	0	8:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	9:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
90977	F	0.1 MG/KG/DAY	DISPOSITION	28	8:46	P	PRIMARY NECROPSY (DAY 28)	
90977	F	0.1 MG/KG/DAY	EYES/EARS/NOSE	21	9:31	P	ABNORMAL PUPIL POSITION LEFT EYE	
90981	F	0.1 MG/KG/DAY	NORMAL	0	8:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	9:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	9:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	7:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
90981	F	0.1 MG/KG/DAY	DISPOSITION	28	8:46	P	PRIMARY NECROPSY (DAY 28)	
90996	F	0.1 MG/KG/DAY	NORMAL	7	9:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	9:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 7

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90996	F	0.1 MG/KG/DAY	NORMAL	28	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90996	F	0.1 MG/KG/DAY	DISPOSITION	28	8:46	P	PRIMARY NECROPSY (DAY 28)
90996	F	0.1 MG/KG/DAY	BODY/INTEG II	0	8:45	P	SCABBING RIGHT EAR
90998	F	0.1 MG/KG/DAY	NORMAL	0	8:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90998	F	0.1 MG/KG/DAY	DISPOSITION	28	8:46	P	PRIMARY NECROPSY (DAY 28)
91011	F	0.1 MG/KG/DAY	NORMAL	0	8:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91011	F	0.1 MG/KG/DAY	DISPOSITION	28	8:46	P	PRIMARY NECROPSY (DAY 28)
91020	F	0.1 MG/KG/DAY	NORMAL	0	8:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91020	F	0.1 MG/KG/DAY	DISPOSITION	28	8:46	P	PRIMARY NECROPSY (DAY 28)
91031	F	0.1 MG/KG/DAY	NORMAL	0	8:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91031	F	0.1 MG/KG/DAY	DISPOSITION	28	8:47	P	PRIMARY NECROPSY (DAY 28)
91033	F	0.1 MG/KG/DAY	NORMAL	0	8:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 8

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
91033	F	0.1 MG/KG/DAY	NORMAL	14	9:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91033	F	0.1 MG/KG/DAY	DISPOSITION	28	8:47	P	PRIMARY NECROPSY (DAY 28)
				0	8:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91035	F	0.1 MG/KG/DAY	NORMAL	14	9:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91035	F	0.1 MG/KG/DAY	DISPOSITION	28	8:47	P	PRIMARY NECROPSY (DAY 28)
				0	8:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91038	F	0.1 MG/KG/DAY	NORMAL	14	9:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91038	F	0.1 MG/KG/DAY	DISPOSITION	28	8:47	P	PRIMARY NECROPSY (DAY 28)
				0	8:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90973	F	3 MG/KG/DAY	NORMAL	14	9:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	8:48	P	PRIMARY NECROPSY (DAY 28)
90973	F	3 MG/KG/DAY	BODY/INTEG II	21	9:40	P	SCABBING RIGHT EAR
				0	8:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90988	F	3 MG/KG/DAY	DISPOSITION	28	8:48	P	PRIMARY NECROPSY (DAY 28)
				7	10:15	P	SCABBING END OF TAIL
				14	9:36	P	SCABBING END OF TAIL
90988	F	3 MG/KG/DAY	BODY/INTEG II	21	9:41	P	SCABBING END OF TAIL
				0	8:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS	
90990	F	3 MG/KG/DAY	NORMAL	7	10:15	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				14	9:36	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				21	9:42	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				28	7:50	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
90990	F	3 MG/KG/DAY	DISPOSITION	28	8:48	P	PRIMARY NECROPSY (DAY 28)	
				0	8:52	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				7	10:16	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				14	9:36	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
90993	F	3 MG/KG/DAY	NORMAL	28	7:51	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				28	8:48	P	PRIMARY NECROPSY (DAY 28)	
				0	8:52	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				7	10:16	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
90993	F	3 MG/KG/DAY	BODY/INTEGUMENT	28	8:48	P	PRIMARY NECROPSY (DAY 28)	
				21	9:42	P	HAIR LOSS FORELIMB(S)	
				0	8:53	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				7	10:16	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
91006	F	3 MG/KG/DAY	NORMAL	28	9:36	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				21	9:43	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				0	8:53	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				7	10:16	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
91006	F	3 MG/KG/DAY	DISPOSITION	28	9:44	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				28	7:52	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				28	8:48	P	PRIMARY NECROPSY (DAY 28)	
				0	8:53	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
91013	F	3 MG/KG/DAY	NORMAL	7	10:17	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				14	9:37	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				21	9:44	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				28	7:52	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
91013	F	3 MG/KG/DAY	DISPOSITION	28	8:48	P	PRIMARY NECROPSY (DAY 28)	
				0	8:54	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				7	10:17	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				14	9:37	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
91017	F	3 MG/KG/DAY	NORMAL	21	9:45	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				28	7:53	P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				28	8:48	P	PRIMARY NECROPSY (DAY 28)	

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 10

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
91023	F	3 MG/KG/DAY	NORMAL	0	8:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91023	F	3 MG/KG/DAY	DISPOSITION	28	8:48	P	PRIMARY NECROPSY (DAY 28)
91032	F	3 MG/KG/DAY	NORMAL	0	8:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	8:48	P	PRIMARY NECROPSY (DAY 28)
91032	F	3 MG/KG/DAY	DISPOSITION	21	9:46	P	HAIR LOSS FORELIMB(S)
91032	F	3 MG/KG/DAY	BODY/INTEGUMENT	0	8:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91034	F	3 MG/KG/DAY	DISPOSITION	28	8:48	P	PRIMARY NECROPSY (DAY 28)
90972	F	30 MG/KG/DAY	NORMAL	0	8:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90972	F	30 MG/KG/DAY	DISPOSITION	35	7:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	8:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	6:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	7:04	P	RECOVERY NECROPSY (WEEK 8)
90976	F	30 MG/KG/DAY	DISPOSITION	0	8:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90976	F	30 MG/KG/DAY	NORMAL	7	10:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90976	F	30 MG/KG/DAY	DISPOSITION	28	8:49	P	PRIMARY NECROPSY (DAY 28)
				0	8:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90978	F	30 MG/KG/DAY	NORMAL	21	9:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	8:49	P	PRIMARY NECROPSY (DAY 28)
				0	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90983	F	30 MG/KG/DAY	DISPOSITION	7	10:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90983	F	30 MG/KG/DAY	NORMAL	28	8:49	P	PRIMARY NECROPSY (DAY 28)
				0	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90987	F	30 MG/KG/DAY	DISPOSITION	21	9:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	8:49	P	PRIMARY NECROPSY (DAY 28)
				0	10:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90987	F	30 MG/KG/DAY	BODY/INTEG II	9	10:58	P	FOUND DEAD
				0	8:58	P	SCABBING MEDIAL TAIL
				0	8:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90987	F	30 MG/KG/DAY	BODY/INTEG II	14	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	8:49	P	PRIMARY NECROPSY (DAY 28)
				21	9:51	P	SCABBING RIGHT EAR
90991	F	30 MG/KG/DAY	NORMAL	0	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 12

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE OBSERVATIONS	
						GRADE	OBSERVATIONS
91001	F	30 MG/KG/DAY	NORMAL	21	9:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	7:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	8:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	6:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	7:04	P	RECOVERY NECROPSY (WEEK 8)
				91003	0	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
91003	F	30 MG/KG/DAY	DISPOSITION	14	9:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	8:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	7:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				42	8:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	6:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	7:04	P	RECOVERY NECROPSY (WEEK 8)
				91004	0	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91004	F	30 MG/KG/DAY	NORMAL	10:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	8:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	8:49	P	PRIMARY NECROPSY (DAY 28)
				91005	0	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	9:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91005	F	30 MG/KG/DAY	DISPOSITION	28	8:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				35	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
91005	F	30 MG/KG/DAY	NORMAL	42	8:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				49	8:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	6:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91005	F	30 MG/KG/DAY	DISPOSITION	57	7:04	P	RECOVERY NECROPSY (WEEK 8)
				0	9:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91007	F	30 MG/KG/DAY	NORMAL	7	10:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91007	F	30 MG/KG/DAY	DISPOSITION	21	9:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				57	7:04	P	RECOVERY NECROPSY (WEEK 8)
91007	F	30 MG/KG/DAY	BEHAVIOR/CNS	49	8:56	P	PARTIAL CLOSURE RIGHT EYE
				35	8:08	P	PURULENT DISCHARGE RIGHT EYE
91007	F	30 MG/KG/DAY	BODY/INTEG II	49	8:56	P	SCABBING FACIAL AREA
				28	8:05	P	SWOLLEN FACIAL AREA
91007	F	30 MG/KG/DAY	SPECIAL	35	8:07	P	MASS, DORSAL TRUNK, 35MM X 17MM X 5MM, SMOOTH, SOFT, IMMOVABLE, NORMAL SURFACE
				35	8:07	P	MASS, DORSAL HEAD, 5MM X 5MM X 5MM, SMOOTH, FIRM, IMMOVABLE, SCABBED, DISCOLORED
91007	F	30 MG/KG/DAY	SPECIAL II	35	8:07	P	MASS, FACIAL AREA, 4MM X 5MM X 3MM, SMOOTH, FIRM, IMMOVABLE, SCABBED, DISCOLORED
				42	8:40	P	MASS, DORSAL TRUNK, 35MM X 17MM X 5MM, SMOOTH, SOFT, IMMOVABLE, NORMAL SURFACE
91007	F	30 MG/KG/DAY	SPECIAL II	42	8:40	P	MASS, DORSAL HEAD, 5MM X 5MM X 5MM, SMOOTH, FIRM, IMMOVABLE, SCABBED, DISCOLORED
				42	8:42	P	MASS, FACIAL AREA, 4MM X 3MM X 2MM, SMOOTH, FIRM, IMMOVABLE, SCABBED, DISCOLORED
91007	F	30 MG/KG/DAY	SPECIAL II	49	9:03	P	MASS, DORSAL NECK, 30MM X 15MM X 12MM, NODULAR, FIRM, MOVABLE, NORMAL SURFACE
				57	6:41	P	MASS, DORSAL NECK, 35MM X 17MM X 10MM, SMOOTH, FIRM, IMMOVABLE, NORMAL SURFACE
				57	6:43	P	MASS, FACIAL AREA, 4MM X 5MM X 3MM, SMOOTH, FIRM,

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS	
91008	F	30 MG/KG/DAY	NORMAL	0	9:01	P	IMMOVABLE, SCABBED, DISCOLORED	
				7	10:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	9:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	8:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				35	8:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				42	8:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				49	9:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	6:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	7:04	P	RECOVERY NECROPSY (WEEK 8)	
91010	F	30 MG/KG/DAY	DISPOSITION	0	9:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	10:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	9:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	8:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				35	8:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				42	8:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				49	9:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	6:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	7:04	P	RECOVERY NECROPSY (WEEK 8)	
91012	F	30 MG/KG/DAY	DISPOSITION	0	9:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	10:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	9:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	8:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	8:49	P	PRIMARY NECROPSY (DAY 28)	
				0	9:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	10:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
<hr/>								

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 15

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS			
91014	F	30 MG/KG/DAY	NORMAL	14	9:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	9:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	8:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				35	8:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				42	8:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				49	9:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	6:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
91014	F	30 MG/KG/DAY	DISPOSITION	57	7:04	P	RECOVERY NECROPSY (WEEK 8)	
91026	F	30 MG/KG/DAY	NORMAL	0	9:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				7	10:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	10:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	8:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	8:49	P	PRIMARY NECROPSY (DAY 28)	
				91027	0	9:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91027	F	30 MG/KG/DAY	DISPOSITION	7	10:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				14	9:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	10:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	8:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	8:49	P	PRIMARY NECROPSY (DAY 28)	
				91029	0	9:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
91029	F	30 MG/KG/DAY	NORMAL	14	9:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				21	10:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				28	8:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				35	8:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				42	8:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				49	9:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	
				57	6:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS	

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207F
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A4 (DETAILED PHYSICAL EXAMINATIONS/DISPOSITIONS - FEMALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 16

STUDY DAYS: 0 THROUGH 57

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
91029	F	30 MG/KG/DAY	DISPOSITION	57	7:05	P	RECOVERY NECROPSY (WEEK 8)
91039	F	30 MG/KG/DAY	NORMAL	0	9:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	10:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	8:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91039	F	30 MG/KG/DAY	DISPOSITION	28	8:49	P	PRIMARY NECROPSY (DAY 28)
91040	F	30 MG/KG/DAY	NORMAL	0	9:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	10:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	9:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	10:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				28	8:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
91040	F	30 MG/KG/DAY	DISPOSITION	28	8:50	P	PRIMARY NECROPSY (DAY 28)

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

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04/21/2008

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 1

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE OBSERVATIONS	
90903	M	0 MG/KG/DAY	NORMAL	0	12:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	9:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	10:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	12:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	9:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90903	M	0 MG/KG/DAY	BODY/INTEG III	22	11:02	P	WET YELLOW MATERIAL UROGENITAL AREA
90905	M	0 MG/KG/DAY	NORMAL	0	12:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
242

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 2

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE OBSERVATIONS	
90905	M	0 MG/KG/DAY	NORMAL	1	12:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	9:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	10:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	9:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90911	M	0 MG/KG/DAY	NORMAL	0	12:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
243

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 3

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE OBSERVATIONS	
90911	M	0 MG/KG/DAY	NORMAL	2	15:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	9:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	10:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	9:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90912	M	0 MG/KG/DAY	BODY/INTEG III	21	9:37	P	WET YELLOW MATERIAL UROGENITAL AREA
				0	12:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
244

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 4

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90912	M	0 MG/KG/DAY	NORMAL	3	11:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	9:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	10:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90915	M	0 MG/KG/DAY	NORMAL	0	12:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 5

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME			GRADE	OBSERVATIONS
90915	M	0 MG/KG/DAY	NORMAL	4	6:47	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				5	6:37	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				6	6:44	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				7	7:19	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				8	11:03	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				9	9:15	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				10	9:59	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				11	7:42	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				12	7:08	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				13	9:23	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				14	10:57	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				15	11:52	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				16	13:01	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				17	11:39	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				18	10:37	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				19	9:24	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				20	9:18	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				21	9:38	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				22	11:03	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				23	7:38	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				24	7:56	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				25	10:37	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				26	8:28	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				27	10:00	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
90917	M	0 MG/KG/DAY	NORMAL	0	12:28	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				1	12:33	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				2	15:09	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				3	11:36	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				4	6:48	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
246

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 6

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90917	M	0 MG/KG/DAY	NORMAL	5	6:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	9:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	10:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90922	M	0 MG/KG/DAY	NORMAL	0	12:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 7

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90922	M	0 MG/KG/DAY	NORMAL	6	6:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	10:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90925	M	0 MG/KG/DAY	NORMAL	0	12:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 8

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY		GRADE	OBSERVATIONS
				DAY	TIME		
90925	M	0 MG/KG/DAY	NORMAL	7	7:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	10:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90929	M	0 MG/KG/DAY	NORMAL	0	12:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
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PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 9

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90929	M	0 MG/KG/DAY	NORMAL	8	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	10:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90929	M	0 MG/KG/DAY	BODY/INTEG III	21	9:41	P	WET YELLOW MATERIAL UROGENITAL AREA
				0	12:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90932	M	0 MG/KG/DAY	NORMAL	7	7:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 10

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90932	M	0 MG/KG/DAY	NORMAL	9	9:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	10:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90939	M	0 MG/KG/DAY	NORMAL	0	12:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 11

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME			GRADE	OBSERVATIONS
90939	M	0 MG/KG/DAY	NORMAL	10	10:02	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				11	7:44	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				12	7:10	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				13	9:26	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				14	11:00	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				15	11:53	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				16	13:04	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				17	11:41	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				18	10:38	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				19	9:25	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				20	9:20	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				21	9:43	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				22	11:05	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				23	7:41	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				24	7:58	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				25	10:39	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				26	8:30	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				27	10:04	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
90940	M	0 MG/KG/DAY	NORMAL	0	12:32	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				1	12:34	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				2	15:11	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				3	11:38	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				4	6:50	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				5	6:39	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				6	6:46	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				7	7:21	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				8	11:05	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				9	9:16	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				10	10:02	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 12

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90940	M	0 MG/KG/DAY	NORMAL	11	7:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90940	M	0 MG/KG/DAY	BODY/INTEG III	21	9:44	P	WET YELLOW MATERIAL UROGENITAL AREA
90942	M	0 MG/KG/DAY	NORMAL	0	12:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 13

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME			GRADE	OBSERVATIONS
90942	M	0 MG/KG/DAY	NORMAL	12	7:11	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				13	9:27	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				14	11:00	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				15	11:54	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				16	13:05	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				17	11:41	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				18	10:39	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				19	9:26	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				20	9:21	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				21	9:44	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				22	11:06	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				23	7:43	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				24	7:59	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				25	10:39	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				26	8:30	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				27	10:06	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
90943	M	0 MG/KG/DAY	NORMAL	0	12:33	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				1	12:34	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				2	15:11	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				3	11:38	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				4	6:50	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				5	6:39	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				6	6:47	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				7	7:21	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				8	11:06	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				9	9:17	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				10	10:03	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				11	7:45	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				12	7:11	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 14

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90943	M	0 MG/KG/DAY	NORMAL	13	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90945	M	0 MG/KG/DAY	NORMAL	0	12:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 15

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE OBSERVATIONS	
						GRADE	OBSERVATIONS
90945	M	0 MG/KG/DAY	NORMAL	14	11:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90953	M	0 MG/KG/DAY	NORMAL	0	12:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
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PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 16

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90953	M	0 MG/KG/DAY	NORMAL	15	11:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				0	12:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90958	M	0 MG/KG/DAY	NORMAL	1	12:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 17

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90958	M	0 MG/KG/DAY	NORMAL	16	13:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90959	M	0 MG/KG/DAY	NORMAL	0	12:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 18

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90959	M	0 MG/KG/DAY	NORMAL	17	11:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	9:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	7:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	10:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	10:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90961	M	0 MG/KG/DAY	NORMAL	0	12:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	6:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	6:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 19

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90961	M	0 MG/KG/DAY	NORMAL	18	10:40 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				19	9:27 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				20	9:23 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				21	9:49 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				22	11:07 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				23	7:45 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				24	8:01 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				25	10:40 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				26	8:31 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				27	10:10 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
90965	M	0 MG/KG/DAY	NORMAL	0	12:37 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				1	12:36 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				2	15:12 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				3	11:40 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				4	6:52 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				5	6:41 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				6	6:48 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				7	7:23 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				8	11:07 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				9	9:18 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				10	10:06 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				11	7:46 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				12	7:12 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				13	9:30 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				14	11:03 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				15	11:56 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				16	13:09 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				17	11:44 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS
				18	10:41 P	NO SIGNIFICANT	CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 20

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME			GRADE	OBSERVATIONS
90965	M	0 MG/KG/DAY	NORMAL	19	9:27	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				20	9:23	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				21	9:49	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				22	11:08	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				23	7:46	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				24	8:01	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				25	10:41	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				26	8:31	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				27	10:10	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
90908	M	0.1 MG/KG/DAY	NORMAL	0	12:39	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				1	12:55	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				2	15:20	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				3	11:57	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				4	7:16	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				5	7:03	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				6	6:49	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				7	7:31	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				8	11:09	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				9	9:36	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				10	10:07	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				11	7:50	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				12	7:14	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				13	9:59	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				14	11:05	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				15	11:57	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				16	13:12	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				17	11:45	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				18	10:41	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				19	9:46	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 21

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90908	M	0.1 MG/KG/DAY	NORMAL	20	9:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90914	M	0.1 MG/KG/DAY	NORMAL	0	12:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	9:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 22

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90914	M	0.1 MG/KG/DAY	NORMAL	21	12:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				0	12:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
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A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 23

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME			GRADE	OBSERVATIONS
90924	M	0.1 MG/KG/DAY	NORMAL	22	11:30	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				23	8:25	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				24	8:32	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				25	11:02	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				26	8:51	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				27	11:05	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
90934	M	0.1 MG/KG/DAY	NORMAL	0	12:41	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				1	12:56	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				2	15:21	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				3	11:58	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				4	7:17	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				5	7:04	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				6	6:50	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				7	7:32	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				8	11:10	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				9	9:37	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				10	10:09	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				11	7:51	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				12	7:14	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				13	10:00	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				14	11:06	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				15	11:58	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				16	13:13	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				17	11:46	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				18	10:42	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				19	9:46	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				20	9:58	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				21	12:50	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				22	11:30	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
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PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 24

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90934	M	0.1 MG/KG/DAY	NORMAL	23	8:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90938	M	0.1 MG/KG/DAY	NORMAL	0	12:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 25

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME			GRADE	OBSERVATIONS
90938	M	0.1 MG/KG/DAY	NORMAL	24	8:33	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				25	11:02	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				26	8:52	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				27	11:06	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
90946	M	0.1 MG/KG/DAY	NORMAL	0	12:42	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				1	12:56	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				2	15:22	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				3	11:58	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				4	7:18	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				5	7:05	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				7	7:32	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				8	11:10	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				9	9:37	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				10	10:10	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				11	7:51	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				12	7:15	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				13	10:01	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				14	11:07	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				15	11:58	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				17	11:47	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				18	10:43	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				19	9:47	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				20	9:59	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				21	12:51	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				22	11:31	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				23	8:26	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				24	8:33	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				25	11:03	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				26	8:52	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 26

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90946	M	0.1 MG/KG/DAY	NORMAL	27	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90946	M	0.1 MG/KG/DAY	BODY/INTEG III	6	6:51	P	DRIED YELLOW MATERIAL UROGENITAL AREA
				16	13:15	P	DRIED YELLOW MATERIAL UROGENITAL AREA
90951	M	0.1 MG/KG/DAY	NORMAL	0	12:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	9:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 27

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME			GRADE	OBSERVATIONS
90951	M	0.1 MG/KG/DAY	NORMAL	26	8:52	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				27	11:08	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
90954	M	0.1 MG/KG/DAY	NORMAL	0	12:43	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				1	12:57	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				2	15:23	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				3	11:58	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				4	7:18	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				5	7:05	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				6	6:51	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				7	7:33	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				8	11:10	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				9	9:37	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				10	10:11	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				11	7:52	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				12	7:16	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				13	10:02	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				14	11:08	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				15	11:59	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				16	13:16	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				17	11:48	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				18	10:43	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				19	9:47	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				20	9:59	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				21	12:53	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				22	11:31	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				23	8:27	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				24	8:34	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				25	11:03	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				26	8:53	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 28

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME			GRADE	OBSERVATIONS
90954	M	0.1 MG/KG/DAY	NORMAL	27	11:08	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
90956	M	0.1 MG/KG/DAY	NORMAL	0	12:43	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				1	12:57	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				2	15:23	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				3	11:58	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				4	7:18	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				5	7:06	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				6	6:52	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				7	7:33	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				8	11:11	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				9	9:38	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				10	10:11	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				11	7:52	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				12	7:16	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				13	10:02	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				14	11:09	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				15	11:59	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				16	13:16	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				17	11:48	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				18	10:43	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				19	9:48	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				20	10:00	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				21	12:53	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				22	11:32	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				23	8:27	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				24	8:34	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				25	11:03	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				26	8:53	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				27	11:09	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 29

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90963	M	0.1 MG/KG/DAY	NORMAL	0	12:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	11:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90907	M	3 MG/KG/DAY	NORMAL	0	12:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
270

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 30

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90907	M	3 MG/KG/DAY	NORMAL	1	12:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	11:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90913	M	3 MG/KG/DAY	NORMAL	0	12:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 31

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90913	M	3 MG/KG/DAY	NORMAL	2	15:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90919	M	3 MG/KG/DAY	NORMAL	0	12:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

WIL-189207
272

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 32

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90919	M	3 MG/KG/DAY	NORMAL	3	12:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	12:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90927	M	3 MG/KG/DAY	NORMAL	0	12:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 33

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90927	M	3 MG/KG/DAY	NORMAL	4	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90948	M	3 MG/KG/DAY	NORMAL	0	12:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 34

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90948	M	3 MG/KG/DAY	NORMAL	5	7:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90949	M	3 MG/KG/DAY	NORMAL	0	12:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 35

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90949	M	3 MG/KG/DAY	NORMAL	6	6:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90960	M	3 MG/KG/DAY	NORMAL	0	12:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 36

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME			GRADE	OBSERVATIONS
90960	M	3 MG/KG/DAY	NORMAL	7	7:36	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				8	11:13	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				9	9:40	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				10	10:16	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				11	7:55	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				12	7:19	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				13	10:06	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				14	11:13	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				15	12:02	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				16	13:21	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				17	11:51	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				18	10:46	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				19	9:50	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				20	10:03	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				21	13:02	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				22	11:35	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				23	8:31	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				24	8:38	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				25	11:05	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				26	8:55	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				27	11:15	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
90966	M	3 MG/KG/DAY	NORMAL	0	12:49	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				1	12:59	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				2	15:26	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				3	12:01	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				4	7:22	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				5	7:09	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				6	6:55	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS
				7	7:36	P	NO SIGNIFICANT	CLINICAL	OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 37

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90966	M	3 MG/KG/DAY	NORMAL	8	11:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90967	M	3 MG/KG/DAY	NORMAL	0	12:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 38

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90967	M	3 MG/KG/DAY	NORMAL	9	9:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90969	M	3 MG/KG/DAY	NORMAL	0	12:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	12:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 39

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90969	M	3 MG/KG/DAY	NORMAL	10	10:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90902	M	30 MG/KG/DAY	NORMAL	0	12:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

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STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90902	M	30 MG/KG/DAY	NORMAL	11	7:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90904	M	30 MG/KG/DAY	NORMAL	0	12:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 41

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90904	M	30 MG/KG/DAY	NORMAL	12	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:47	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90904	M	30 MG/KG/DAY	EYES/EARS/NOSE	22	11:37	P	DRIED RED MATERIAL AROUND NOSE
90906	M	30 MG/KG/DAY	NORMAL	0	12:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 42

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90906	M	30 MG/KG/DAY	NORMAL	13	10:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90910	M	30 MG/KG/DAY	NORMAL	0	12:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 43

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90910	M	30 MG/KG/DAY	NORMAL	15	12:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:35	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90910	M	30 MG/KG/DAY	BODY/INTEG III	9	9:42	P	DRIED YELLOW MATERIAL UROGENITAL AREA
90920	M	30 MG/KG/DAY	NORMAL	0	12:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 44

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90920	M	30 MG/KG/DAY	NORMAL	15	12:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90923	M	30 MG/KG/DAY	NORMAL	0	12:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 45

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90923	M	30 MG/KG/DAY	NORMAL	16	13:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:48	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90926	M	30 MG/KG/DAY	NORMAL	0	12:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 46

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY			
				DAY	TIME	GRADE	OBSERVATIONS
90926	M	30 MG/KG/DAY	NORMAL	17	11:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:36	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90930	M	30 MG/KG/DAY	NORMAL	0	12:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 47

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90930	M	30 MG/KG/DAY	NORMAL	18	10:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90931	M	30 MG/KG/DAY	NORMAL	0	12:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 48

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90931	M	30 MG/KG/DAY	NORMAL	19	9:53	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90935	M	30 MG/KG/DAY	NORMAL	0	12:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:49	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 49

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90935	M	30 MG/KG/DAY	NORMAL	20	10:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:37	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90937	M	30 MG/KG/DAY	NORMAL	0	12:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	7:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:54	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 50

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90937	M	30 MG/KG/DAY	NORMAL	21	13:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90941	M	30 MG/KG/DAY	NORMAL	0	12:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	6:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	8:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 51

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90941	M	30 MG/KG/DAY	NORMAL	22	11:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:38	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90944	M	30 MG/KG/DAY	NORMAL	0	12:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	7:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:17	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	8:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 52

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90944	M	30 MG/KG/DAY	NORMAL	23	8:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90947	M	30 MG/KG/DAY	NORMAL	0	12:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	7:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	8:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:50	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 53

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90947	M	30 MG/KG/DAY	NORMAL	25	11:09	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90947	M	30 MG/KG/DAY	BODY/INTEG III	21	13:17	P	WET YELLOW MATERIAL UROGENITAL AREA
90950	M	30 MG/KG/DAY	NORMAL	0	12:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	7:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:44	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	8:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:55	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:39	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 54

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90950	M	30 MG/KG/DAY	NORMAL	25	11:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	8:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90952	M	30 MG/KG/DAY	NORMAL	0	12:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:03	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	7:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:26	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	8:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:14	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:20	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:18	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 55

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE	OBSERVATIONS
90952	M	30 MG/KG/DAY	NORMAL	26	9:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90955	M	30 MG/KG/DAY	NORMAL	0	12:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	7:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	8:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	9:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 56

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
					TIME	GRADE	OBSERVATIONS
90955	M	30 MG/KG/DAY	NORMAL	27	11:29	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90962	M	30 MG/KG/DAY	NORMAL	0	13:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:05	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	7:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:27	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	8:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:15	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:07	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:51	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:12	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:40	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:10	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	9:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 57

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME GRADE OBSERVATIONS		
90964	M	30 MG/KG/DAY	NORMAL	0	13:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				1	13:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	7:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	8:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:21	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:32	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:58	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:56	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:23	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:42	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	9:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:30	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
90964	M	30 MG/KG/DAY	BODY/INTEG III	9	9:45	P	DRIED YELLOW MATERIAL UROGENITAL AREA
90968	M	30 MG/KG/DAY	NORMAL	0	13:01	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

A 28-Day Oral (Gavage) Toxicity Study
Of H-28397 In Mice With A 28-Day Recovery

DuPont-24459

PROJECT NO.: WIL-189207M
SPONSOR: E.I. DUPONT
SPONSOR NO.: DUPONT-24459

TABLE A5 (AT TIME OF DOSING - MALES)
A 28-DAY ORAL STUDY OF H-28397 IN MICE
INDIVIDUAL CLINICAL OBSERVATIONS

PAGE 58

STUDY DAYS: 0 THROUGH 27

ANIMAL	SEX	GROUP	CATEGORY	STUDY DAY	TIME	GRADE OBSERVATIONS	
90968	M	30 MG/KG/DAY	NORMAL	1	13:04	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				2	15:34	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				3	12:06	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				4	7:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				5	7:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				6	7:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				7	7:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				8	11:19	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				9	9:45	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				10	10:28	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				11	8:02	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				12	7:25	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				13	10:16	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				14	11:22	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				15	12:08	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				16	13:33	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				17	11:59	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				18	10:52	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				19	9:57	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				20	10:13	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				21	13:24	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				22	11:43	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				23	8:41	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				24	8:46	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				25	11:11	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				26	9:00	P	NO SIGNIFICANT CLINICAL OBSERVATIONS
				27	11:31	P	NO SIGNIFICANT CLINICAL OBSERVATIONS

GRADE CODE: 1 - SLIGHT 2 - MODERATE 3 - SEVERE P - PRESENT

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04/21/2008

WIL-189207
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